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Differences in depression symptoms in patients with Alzheimer's and Parkinson's diseases:

evidence from the 15-item Geriatric Depression Scale (GDS-15)

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SUMMARY

Objective—Depression occurs frequently in patients with both Alzheimer's disease (AD) and Parkinson's disease (PD), but there has been little comparison of depression symptoms in the two populations.

Method—The 15-item Geriatric Depression Scale (GDS-15) was administered as a depression screening instrument to 232 AD patients and 266 PD specialty care patients with at most mild dementia. Logistic regression models were used to determine disease-specific associations with individual GDS-15 items, and factor analysis was used to assess GDS-15 factor structure in the two populations.

Results—Controlling for total GDS-15 score and other covariates, AD patients reported more dissatisfaction with life ($p = 0.03$) and memory problems ($p < 0.001$), while PD patients reported more fearfulness ($p = 0.01$), helplessness ($p < 0.01$), a preference to stay at home ($p = 0.02$), and diminished energy ($p < 0.01$). Three factors were generated in PD (explaining 55% of the total variance) and five in AD (explaining 59% of the total variance), and the two main factors generated in both populations related primarily to unhappiness and negative thoughts.

Conclusions—The factor structure of the GDS-15 is similar in AD and PD patients with at most mild stage dementia, but between-group differences on 6 of the GDS-15 items suggests the non-specificity of certain items in the two populations.

Keywords

rating scale; depression; Alzheimer's disease; Parkinson's disease; Geriatric Depression Scale

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INTRODUCTION

Alzheimer's disease (AD) and Parkinson's disease (PD) are the two most common neurodegenerative diseases (Olanow *et al*., 2001; Hebert *et al*., 2003). Up to 40% of patients with AD and PD have major or minor depression (Olin *et al*., 2002; Weintraub and Stern, 2005), but questions remain about what symptoms constitute depression in these two populations. Experts' concerns about the appropriateness of some Diagnostic and Statistical Manual (DSM-IV-TR) (APA, 2000) depression criteria led experts to propose modified criteria for depression in AD (Olin *et al*., 2002). Their proposed changes included emphasizing loss of pleasure over loss of interest (as the latter was thought to be commonly a symptom of apathy instead of depression), inclusion of irritability as a symptom of depression, removing diminished ability to think or concentrate as a symptom, and decreasing the total number of symptoms required to meet criteria for a diagnosis of depression.

Similar concerns exist over the symptoms of depression in PD, particularly due to symptom overlap. Specifically, certain symptoms (e.g. fatigue, insomnia, psychomotor changes, and loss of concentration) can either signify depression or be core PD symptoms (Weintraub and Stern, 2005). In a study (Ehrt *et al*., 2006) comparing non-demented depressed patients with and without PD, PD patients reported less sadness, less anhedonia, less feelings of guilt, but more concentration problems than depressed control subjects. Concerns about the DSM-IV-TR criteria as applied to depression in PD led to a proposal for provisional modifications in this population (Marsh *et al*., 2006), including the use of an inclusive scoring approach, the inclusion of subsyndromal depression in research studies, the specification of timing of assessments in patients with motor fluctuations, and the use of informants for cognitively impaired patients.

Little published research exists to inform revising the criteria for depression in PD and AD, and few studies have compared the presentation of depression symptoms in these two disease states. One study of patients with either AD or PD (Naarding *et al*., 2002) found differences in the optimal performance of the Hamilton Depression Rating Scale (HAM-D) cutoff scores for screening, diagnosis, and dichotomization of depression in the two populations, but differences in the endorsement of specific items were not presented.

To better understand whether and how depression symptoms differ among persons with AD and PD, we examined the performance of the 15-item Geriatric Depression Scale (GDS-15) (Sheikh and Yesavage, 1986) in two cohorts of outpatients, one with AD and the other with PD. We selected the GDS-15 because it is a commonly-used, self-report depression screening instrument. Compared with many other depression rating scales, it de-emphasizes the somatic symptoms of depression and instead focuses on the psychological symptoms of depression. The GDS-15 has been validated for use in both AD (Müller-Thomsen *et al*., 2005) and PD (Weintraub *et al*., 2006); although there are concerns that the GDS may perform suboptimally in patients with more severe cognitive impairment (Burke *et al*., 1989; Feher *et al*., 1992; Gilley and Wilson, 1997; Müller-Thomsen *et al*., 2005), it has been reported to perform adequately in AD patients with at most mild stage AD (Brodaty and Luscombe, 1996). Using regression analyses and factor analyses, we hypothesized that the depression factors generated in the two populations would be similar, but that there would be disease-specific differences in the endorsement of specific items.

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METHODS

Participants

Study participants were patients with a diagnosis of either AD or idiopathic PD. AD patients (n = 232) were receiving specialty care at the Alzheimer's Disease Core Center (ADCC) at the University of Pennsylvania. The AD diagnosis was made at consensus conference using NINCDS-ADRDA criteria for probable or possible AD (McKhann *et al*., 1984). PD patients (n = 264) were receiving specialty care at the Parkinson's Disease Centers at the University of Pennsylvania (n = 187) or the Philadelphia Veterans Affairs Medical Center (n = 77). A diagnosis of possible or probable idiopathic PD (Gelb *et al*., 1999) was made by a movement disorders specialist.

The collection of the data was approved by the Institutional Review Boards at the University of Pennsylvania and the Philadelphia Veterans Affairs Medical Center, and all patients provided written informed consent.

Data collection and measures

The GDS-15 was used as a self-report (i.e. proxy informants were not used) instrument. A GDS-15 score ≥5 was used to characterize patients as having clinically-significant depression, which is similar to cutoffs previously used in PD (Weintraub *et al*., 2006) and AD (Müller-Thomsen *et al*., 2005). The Mini-Mental State Examination (MMSE) (Folstein *et al*., 1975) was administered as a measure of global cognition.

For AD patients attending the ADCC, a psychometric tester administered the MMSE, and the clinician administered the GDS during their assessment of the patient. For PD patients, the GDS questions were asked and patients' responses recorded by a trained research assistant as part of a study screening for depression in PD. At the same time, the research assistant also administered the MMSE. As research suggests that the GDS performs best in AD in patients with at most mild stage AD (Brodaty and Luscombe, 1996), we included only subjects in each population with an MMSE score ≥18 (PD range = 18-30, AD range = 20-30).

Analysis

Between-group differences on demographic and clinical variables were examined using two-sample t-test with Levene's test for equality of variances or Mann-Whitney U test (for continuous variables), and the chi-square test (for categorical variables). Logistic regression models were used to examine the effect of group status (AD or PD) on individual GDS-15 item scores. The corresponding Wald test p values were reported. For each of these models, the score on the individual GDS-15 item was the dependent variable, with group status, total GDS score (minus the individual GDS-15 item that was the dependent variable for that model), age, sex, educational level, and MMSE score entered as the independent variables. Factor analysis (principal components) was run with all 15 individual GDS items entered simultaneously. Factors with eigenvalues >1 were retained after analysis with varimax rotation. All statistical tests were two-sided. All analyses were conducted with SPSS 14.0 (SPSS, 2006).

RESULTS

Demographic and clinical characteristics

Table 1 shows that AD patients on average were older, more likely to be female, less likely to be white, and had a slightly lower educational level than PD patients. PD subjects on average had a significantly higher GDS-15 score than AD patients (4.2 ± 4.0 *vs* 2.3 ± 2.5 [Z = -5.2, p < 0.001] respectively), and 34% of PD patients = and 16% of AD patients were depressed based on their GDS-15 score (X^2[df] = 19.0[1], p < 0.001).

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Factor analyses

Table 2 shows that factor analysis identified three factors in PD that accounted for 55% of the total variance. The first factor loaded nine of the GDS-15 items. Among patients with AD, five factors were identified that accounted for 59% of the total variance, and no individual factor loaded more than four items in this population.

To determine the effect that between-group differences in demographic factors may have had on the results of the factor analyses, all factor analyses were re-run after dividing each group first by sex, then age, then education, and finally MMSE score (the latter three dichotomized at the median). Analyses were not re-run to control for race, as subjects were overwhelming white. The second set of analyses produced factor structures that were very similar to those initially generated (results not presented), suggesting that baseline differences in demographic factors did not influence the outcome of the factor analyses.

Group effect on GDS-15 item scores

Logistic regression models found that 6 of the 15 GDS items showed between-group differences (Table 3). Specifically, regardless of overall severity of depression, PD patients were more likely than AD patients to report fearfulness, helplessness, and a preference to stay at home, and less likely to report feeling full of energy. AD patients were more likely to report having memory problems and less likely to report feeling satisfied with life.

DISCUSSION

Our results demonstrate that the GDS-15 has similar factor structures in both AD and PD, but that there are between-population differences in the endorsement of specific GDS-15 items.

There are several limitations to this study. First, the AD and PD populations were taken from different centers, though all three sites were tertiary care clinical research centers at the same institution. Second, we were not able to examine the sensitivity, specificity, and positive or negative predictive value of the GDS-15 in AD and PD, as no gold standard diagnosis of depression was made. Third, total GDS-15 scores were lower and had less variability in the AD patients, which may have affected the results of our logistic regression and factor analysis models due to less frequent endorsement of symptoms. It is unclear why AD patients were less depressed on average than PD patients; the mean GDS-15 score in PD patients was similar to that reported in a previous epidemiological study (Meara *et al*., 1999), but the average score in our AD sample was lower than that previously reported (Müller-Thomsen *et al*., 2005). Related to this, we did not have data on the percentage of patients that were being treated for depression. Fourth, we did not include a control group of elderly patients without PD or AD, so we cannot directly compare GDS-15 performance in patients with and without neurodegenerative disease. Finally, the GDS-15 only covers three of the nine DSM-IV symptoms for major depressive episode, so our results are simply a comparison of GDS-15 performance in PD and AD, not a comparison of the overall construct of depression in the two populations.

We found differences, even after controlling for overall depression severity, between AD and PD patients on six of the GDS-15 items. Inspection of these items suggests that certain GDS-15 items are non-specific for depression in AD and PD. For instance, diminished energy was more common in PD than AD, and it is well-reported that fatigue and sleepiness are very common in PD regardless of depression (Hobson *et al*., 2005). A similar argument could be made for the more frequent occurrence of memory complaints in AD patients. The explanation that certain GDS-15 items are non-specific in AD or PD is speculative, as subjects were not administered a structured clinical interview to diagnose depression.

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Regarding the factor analyses, the items that loaded on Factor 1 in both AD and PD mostly related to unhappiness (i.e. mood disturbance), and the items that loaded on Factor 2 (and Factor 3 in AD) related to negative thoughts associated with depression. In contrast, the items on Factor 3 in PD and Factors 4 and 5 in AD either occur commonly as core symptoms of each disease or might be a direct psychosocial consequence of having the respective illness.

The results of the factor analysis for the GDS-15 in PD and AD were similar to that reported in a recent large-scale factor analysis of the GDS-15 in nearly 1,000 elderly patients in a variety of settings (Onishi *et al*., 2006). In this study four GDS-15 factors were generated: (1) unhappiness (items 1, 5, 7 and 11); (2) apathy and anxiety (items 2, 3, 4, 6, 8, and 15); (3) loss of hope and morale (items 9, 10, 12, and 14); and (4) energy loss (item 13). This suggests that other than some disease-specific differences in several of the GDS-15 items, the overall factor structure for the instrument in PD and AD is similar to that in the elderly population at large.

In conclusion, the primary factors generated from the GDS-15 in both PD and AD relate to unhappiness and negative thoughts, suggesting that the instrument performs similarly in the two populations and to elderly patients in general. However, results also suggest that certain GDS-15 items are non-specific for depression in AD or PD. Further research can clarify this issue by examining the association between individual GDS-15 items and a formal diagnosis of depression in AD and PD, which ultimately will help in the development of disease-specific depression criteria and rating scales.

KEY POINTS

- Controlling for severity of depression, AD patients report more dissatisfaction with life and memory problems than PD patients.
- Controlling for severity of depression, PD patients report more fearfulness, helplessness, a preference to stay at home, and diminished energy than AD patients.
- The primary GDS-15 factors in both AD and PD relate primarily to unhappiness and negative thoughts.

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Table 1

Demographic and clinical characteristics

Variable	PD (*n*=266)	AD (*n*=232)	Test statistic	*P*-value (df)[a]
Age (mean [SD] years)	68.2 (10.2)	76.0 (8.0)	*t*=-9.6	<0.001 (489.0)
Sex (% male)	69.3	40.5	X^2=41.5	<0.001 (1)
Race (% white)	96.2	88.7	X^2=10.2	0.001 (1)
Education (mean [SD] years)	14.8 (3.2)	14.1 (3.3)	*t*=2.4	0.02 (491)
MMSE (mean [SD] score)	28.4 (1.8)	23.8 (2.4)	*t*=23.5	<0.001 (422.4)
Depression				
GDS-15 (mean [SD] total score)	4.2 (4.0)	2.3 (2.5)	Z=-5.2	<0.001
Non-Depressed (% yes)[b]	66.4	83.6	X^2=25.2	<0.001 (2)
Mild Depression[c] (% yes)	19.9	14.2		
Moderate-Severe Depression[d] (% yes)	13.7	2.2		

[a] *T*-test with Levene's test for equality of variances or Mann-Whitney *U*-test (for continuous variables), chi-square test (for categorical variables)

[b] GDS-15 score <5

[c] GDS-15 score ≥5 and <10

[d] GDS-15 score ≥10.

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Table 2

Factor analysis of GDS-15 in PD and AD[a]

Item #	Item Content	Parkinson's disease[b]			Alzheimer's disease[c]				
		Factor 1	Factor 2	Factor 3	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
1	Satisfied with life	0.73	—	—	0.71	—	—	—	—
2	Dropped many activities and interests	—	—	0.74	—	—	—	—	0.50
3	Life is empty	0.74	—	—	—	0.73	—	—	—
4	Often get bored	—	0.52	—	—	0.59	—	—	—
5	Good spirits most of time	0.72	—	—	0.74	—	—	—	—
6	Afraid something bad is going to happen	—	0.59	—	—	—	—	0.82	—
7	Feel happy most of time	0.79	—	—	0.84	—	—	—	—
8	Often feel helpless	0.42	0.54	—	—	—	0.80	—	—
9	Prefer to stay at home	—	—	0.75	—	—	—	—	0.85
10	More problems with memory than others	—	0.74	—	—	—	—	0.55	—
11	Wonderful to be alive	0.71	—	—	—	—	—	0.48	—
12	Feel pretty worthless	0.49	0.47	—	—	0.45	0.53	—	—
13	Full of energy	—	—	0.59	0.51	—	—	—	—
14	Situation is hopeless	0.48	0.43	—	—	—	0.66	—	—
15	Most people better off than you	0.43	0.47	—	—	0.78	—	—	—

[a] Only items with factor loading ≥0.40 included

[b] Explains 54.5% of variance

[c] Explains 59.3% of variance.

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Table 3

GDS-15 Performance in PD and AD by individual item[a]

Item	Item Content	Percentage (%) Endorsing Item Toward Depression		Model X^2 (P value[b])	Group Effect	
		PD	AD		B (SE)	Wald (p-value[c])
1	Satisfied with life[d]	24.4	13.4	193.3 (<0.001)	-1.0 (0.47)	4.9 (.03)[e]
2	Dropped many activities and interests	38.7	30.6	149.5 (<0.001)	0.4 (0.36)	1.3 (.26)
3	Life is empty	13.8	12.1	163.7 (<0.001)	-0.6 (0.49)	1.4 (.21)
4	Often get bored	28.6	17.2	135.5 (<0.001)	0.5 (0.42)	1.7 (.20)
5	Good spirits most of time[d]	23.3	6.5	201.0 (<0.001)	0.4 (0.54)	0.5 (.49)
6	Afraid something bad is going to happen	25.2	7.3	81.7 (<0.001)	1.2 (0.45)	6.8 (.01)[f]
7	Feel happy most of time[d]	28.9	13.4	209.3 (<0.001)	-0.3 (0.46)	0.5 (.50)
8	Often feel helpless	27.1	6.5	167.4 (<0.001)	1.7 (0.52)	10.1 (<0.01)[f]
9	Prefer to stay at home	43.2	23.7	77.2 (<0.001)	0.8 (0.33)	5.6 (.02)[f]
10	More problems with memory than others	29.3	43.5	70.7 (<0.001)	-1.3 (.33)	15.5 (<0.001)[e]
11	Wonderful to be alive[d]	14.7	4.3	117.0 (<0.001)	0.8 (0.60)	1.7 (.20)
12	Feel pretty worthless	22.2	11.2	193.8 (<0.001)	0.5 (0.50)	0.9 (.34)
13	Full of energy[d]	63.2	26.7	175.8 (<0.001)	1.1 (0.34)	9.6 (<0.01)[f]
14	Situation is hopeless	15.8	7.8	109.5 (<0.001)	-0.1 (0.51)	0.1 (.80)
15	Most people better off than you	14.3	8.2	101.9 (<0.001)	-0.9 (0.53)	2.9 (.09)

[a] Logistic regression model controlling for total GDS score, age, sex, educational level, and MMSE score

[b] Degrees of freedom (df)=six for each model

[c] Degrees of freedom (df)=one for each group effect

[d] Item reverse coded

[e] Symptom associated with Alzheimer's disease

[f] Symptom associated with Parkinson's disease.

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