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Self-reported Distress after Cognitive Testing in Patients with Alzheimer's Disease

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Abstract

Background—The prevalence and degree of self-reported distress that patients with Alzheimer's disease (AD) experience after cognitive testing remains unknown. It is also unknown whether this level of distress is at all related to specific patient factors, test performance, or awareness of test performance.

Methods—In 154 mild-moderate AD patients and 62 cognitively intact patients, we measured self-reported distress, on a five point Likert scale, after 45 minutes of cognitive testing. Using multivariate logistic regression, we then examined whether demographic factors, level of education, depressive symptoms, cognitive performance, perceived test difficulty, and perceived test performance compared to 10 years ago were predictive of self-reported distress.

Results—The prevalence of any self-reported distress in patients with AD was 70% compared to 47% in patients without AD ($P < .001$). Of those with AD, bivariate analyses revealed that patients who reported more difficulty with testing (RR 1.32, 95% CI 1.25–1.37) and felt they performed worse than 10 years ago (RR 1.21, 95% CI 1.07–1.30) were at increased risk for reporting more distress. Paradoxically, cognitive performance was a weak predictor of distress, with only language performance demonstrating an association (RR 0.95, 95% CI 0.89–0.99). Adjustments for demographic factors, education, dementia severity, or depressive symptoms in the multivariable analyses, did not alter these relationships.

Conclusion—Cognitive tasks provoke more distress in patients with mild-moderate AD compared with persons who do not have dementia. Predictors of distress are more closely related to patient awareness about test difficulty and performance, rather than actual test performance.

INTRODUCTION

Cognitive testing is essential to Alzheimer's disease (AD) research and care. It provides clinicians and clinical investigators with a measure of a patient's cognitive function that they can use together with clinical data to diagnose and follow the progression of AD (1–3) and to assess the efficacy of an intervention to prevent or treat AD in clinical trials. (4)

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As valuable as cognitive testing is for diagnosis, treatment, and staging, clinical experience shows that such cognitive tasks may also negatively impact a patient's psychological state. This is particularly evident in patients aware of their cognitive impairments who must confront their own deficits. Although those with dementia often lose awareness of their cognitive deficits as their condition declines (5), many patients, particularly those in the earlier stages, do not. (6)

Few empiric studies describe the relationship between cognitive testing and distress in the patients who undergo it. (7) By quantifying this association and defining the demographic and disease factors that predict this distress, clinicians may generate valuable information that could alter the management of patients with AD in at least two ways. First, patients who experience distress when exposed to a standardized cognitive challenge also may be at greater risk for experiencing high levels of distress when performing more ecologically valid cognitive tasks, such as managing one's finances or preparing a meal. Second, clinicians who identify factors that predict distress after cognitive testing can anticipate this symptom and develop ways to mitigate its impact.

This study represents the first step in a line of investigation designed to determine the clinical value of measuring the psychological responses patients have to cognitive tasks. We examine the prevalence and severity of self-reported distress after a cognitive test battery in patients with and without AD, Furthermore, we determine patient factors associated with this distress, and tested whether actual test performance or patient perceptions of test performance are related the degree of distress patients report.

METHODS

Participants

Data for this study were gathered from participants enrolled in the cohort of the PENN Memory Center of the Alzheimer's Disease Center at the University of Pennsylvania. All 154 patients with AD met the NINCDS-ADRDA criteria for probable or possible AD and had mild to moderate stage disease based on a Folstein mini-mental status exam (8) score between 12 and 30. All 62 cognitively intact persons did not meet criteria for the diagnosis of dementia or mild cognitive impairment following a clinical history and exam. Informed consent was obtained from all participants, or their proxies when necessary. The University of Pennsylvania Institutional Review Board approved the cohort study.

Data Collection

As part of routine annual assessments, a trained research assistant administered a cognitive test battery to subjects. The battery takes 45 minutes to complete and consists of the following measures: Verbal Fluency Test (9), Boston Naming Test (10), Folstein Mini Mental State exam, Word List Memory Task (11), Delayed Word List Recall (11), Word List Recognition (11), Logical Memory 1 (12), Clock Drawing Task (13), Digit Symbol Test (14), and the Logical Memory 2 (12). Clinicians collected data on age, race, ethnicity, and years of education, and assessed self-reported depressive symptoms using the 15-item Geriatric Depression Scale (GDS). (15) Knowledgeable informants for the participants with AD also completed the Dementia Severity Rating Scale (DSRS). (16)

Self-reported measures

Immediately following the cognitive test battery, a research assistant asked the participants "What was it like answering these questions? Would you say… not at all distressing, mildly distressing, moderately distressing, very distressing, or extremely distressing." To assess for perceptions of test difficulty, participants were also asked, "What was it like answering these

questions? Would you say… very easy, easy, somewhat easy, somewhat difficult, difficult, or very difficult." To assess the participants' level of awareness in their test performance, they were asked, "How is your ability to do these tests compared to ten years ago? Better than ten years ago, the same as ten years ago, or worse than ten years ago."

Statistical analysis

Because patients rarely reported having extreme distress, we collapsed the "very" and "extremely" distressing categories into a single, "severe" category. All subsequent analyses evaluated the degree of self-reported distress using this ordinal four category scale. For similar reasons, we collapsed patients' perceptions of test difficulty into two categories: "very to somewhat easy" and "very to somewhat difficult." To enhance the clinical interpretation of patient perceptions of historical test performance, we combined the categories of patients who reported having the "same" or "better" test performance compared to 10 years ago. For patients with AD, we operationalized that reporting test performance that was "worse than ten years ago" signified adequate insight with respect to their cognitive abilities. Meanwhile, responses of "same" or "better" test performance signified impaired insight, as persons with AD, by definition, have a clinically significant decline in their cognitive performance.

The neuropsychiatric tests were separated into four cognitive domains: language, memory, processing speed, and visual-spatial ability. Raw scores for the tests in each domain were converted into Z-scores and summed to form four composite variables. A composite variable, representing the sum of all test Z-scores, was also created to provide a measure of overall test performance in patients with AD. (17)

For comparisons between AD and intact patients, we used the Chi square statistic for categorical data, an unpooled Student's t-test for normally distributed data, and the Wilcoxon rank sum test for variables with non-normal distributions as determined by the Shapiro-Wilk test. Bivariate and multivariable analyses were assessed using ordinal logistic regression. (18) All odds ratios were converted to relative risk (RR) estimates, as the presence of self-reported distress was common (>10%). (19)

Using a manual stepwise procedure, we performed two sets of multivariable analyses. First, we examined the relationship between perceptions of test difficulty and test performance on self-reported distress given the potential confounding factors of age, gender, race, education, dementia severity, actual test performance, and GDS score. Second, we evaluated the relationship between test performance in each of the specific cognitive domains and self-reported distress. In these models, domain performance was controlled for age, gender, race, education, dementia severity, and GDS score. Variables included in the final models were either statistically significant at the $P < .05$ level or were associated with greater than a ten percent change in the parameter estimate of the independent variable or variables of interest. All analyses were performed using SAS, version 9.1 (SAS Institute, Inc., Cary, NC)

RESULTS

Table 1 compares the demographics, cognitive test performance, perceptions of cognitive performance and test difficulty, and the degrees of distress reported after testing between patients with AD and cognitively intact older adults. As expected, patients with AD had an average MMSE score that was lower than the mean score of the cognitively intact group. Similarly, the AD patients had significantly lower performance on all other measures of cognitive ability ($P < .001$). They also tended to be older ($P = .002$) and to have fewer years of education ($P = .002$) than the intact group. Both groups had a similar gender (>63% female), racial (>65% white), and ethnic mix (>84% non-Latino), and both groups were well educated, having an average of at least 12 years of education. Although the patients with AD reported

more depressive symptoms (P < .001) than the cognitively intact group with significantly higher scores on the GDS, the medians for both the AD and intact groups were low (1 and 0, respectively).

The prevalence and severity of self-reported distress

Nearly three-quarters (70%, n=108/154) of the patients with AD reported distress following cognitive testing. The majority of patients (53%) categorized their distress as mild to moderate severity, and a much smaller percentage (17%) found the experience to be very or extremely distressing. Only 47% of the cognitively intact patients reported experiencing distress after testing (P < .001). The severity of their distress was also significantly lower with fewer percentages of patients reporting moderate and severe degrees of distress (16% versus 23% and 2% versus 17%, respectively; P = .002).

Predictors of distress in patients with AD

In the bivariate analyses (table 2), patients with AD who perceived the testing to be more difficult had a significantly greater risk of reporting more distress (RR 1.32, 95% CI 1.25–1.37) than those who did not find testing difficult. AD patients who felt they performed worse than 10 years ago (RR 1.21, 95% CI 1.07–1.30) also had an increased risk of reporting more distress than those who felt they did the same or better than 10 years ago. Patients who admitted having, “more problems with memory than most” on the GDS, however, did not have a greater risk of reporting more distress (RR 1.12, 95% CI .95–1.24). Of the four cognitive domains shown in table 3, we observed a small but statistically significant bivariate association between decreased language ability and self-reported distress (RR 0.95, 95% CI 0.89–0.99). Within the cognitively intact group, however, there were no significant bivariate associations between demographic factors, cognitive test performance, perceptions of test difficulty or test performance, and increasing levels of reported distress.

In the multivariate analyses, patients with AD were significantly more likely than those without AD to report distress, after adjusting for age, education, and GDS scores (RR 1.26, 95% CI 1.14–1.33). Among patients with AD (table 2), patients who perceived the tests to be more difficult (RR 1.32, 95% CI 1.22–1.38) and believed that they performed worse than 10 years ago (RR 1.25 95% CI 1.08–1.34) had an increased risk of reporting more distress after adjusting for age, education, race, cognitive test performance, and GDS scores. The multivariate analysis also revealed that patients who were white were also at increased risk of reporting greater levels of distress than non-white patients with AD (RR 1.29 95% CI 1.06–1.38). Lastly, despite adjustment for potential confounders, the language domain remained the only measure of actual test performance that was a significant predictor of distress (table 3).

DISCUSSION

Among patients with mild to moderate Alzheimer’s disease, self-reported distress following cognitive testing is common. Nearly three-quarters (70%) of patients in our sample reported some form of distress. Distress, however, is also common among persons who are cognitively intact. Nearly half (47%) of our non-demented comparison group reported it. However, it was significantly lower in prevalence and in severity than that found among persons with AD. While there were no predictors of self-reported distress in the cognitively intact group, patients with AD had several. Namely, those who were white, had lower performance on tests of language ability, were more aware of their cognitive declines, and perceived the tests to be more difficult, all had a greater risk of reporting distress.

These findings have two clinical implications. First, neuropsychological testing is not necessarily a benign exercise, but may have short term psychological effects. These effects

may generate anxiety and potentially influence patients' compliance with follow-up, as is observed with patients who experience distress following testing for other diseases.(20) Knowledge of this distress, however, provides clinicians with the opportunity to prepare patients and family members for the risks associated with testing and to institute precautions after testing to minimize its effect. Furthermore, these data provide a starting point for establishing a phenotype for patients with AD. This may then be used to better identify patients at risk for experiencing excessive levels of distress.

Second, patients with AD who experience distress during testing may also experience similar distress while performing other functionally relevant tasks, such as balancing a checkbook or following a recipe. These tasks simulate the same kind of cognitive challenges experienced in neuropsychological testing. Therefore, self-reported distress during testing may serve as a marker for those patients with AD who may have a more chronic exposure to distress. The absence of data on the outcomes associated with symptoms of distress in patients with AD represents a clinically relevant area of future research.

Regarding risk factors for distress, insight into cognitive problems emerged as a predictor. At least 60% of the patients with AD reported that they performed "worse" on the testing compared to 10 years ago. Given that insight has also been associated with a greater likelihood of being capable of giving consent for an AD treatment (21), our results suggest that one may derive both scientific and clinical value from assessing patient insight.

Paradoxically, actual cognitive test performance was minimally associated with experiencing distress. Only performance in language ability was associated with distress. Furthermore, our informant based measure of dementia severity, the DSRS, also failed to show an association with self-reported distress. This suggests that the presence of distress may not necessarily be linked to the severity of functional or cognitive ability. One potential explanation for this is that the patients with AD who perceived greater test difficulty and had greater insight into their deficits had small declines in cognitive ability for the tests used in this study. Tests of other cognitive domains or with a higher sensitivity for detecting change may have revealed a stronger association between insight and distress and actual performance and distress.

Although there was a surprisingly modest relationship between actual cognitive performance and self-reported distress, our findings remain consistent with existing hypotheses linking exposure to stress with hippocampal (22,23) and prefrontal cortex (24) dysfunction. Namely, we observed an association between language ability, a cognitive function associated with the prefrontal cortex, (25) and distress. We did not, however, demonstrate a relationship between performance on memory domain tests and self-reported distress. Differences in the types of tests used to measure episodic and declarative memory in previous studies may, in part, explain the absence of this observation. Additionally, given the high distribution of scores in the lower ranges for the tests of logical memory 1 & 2 and word list recall (table 1), our memory domain measure may have been limited in its ability to discriminate memory function due to floor effects.

The absence of baseline measurements of self-reported distress taken prior to the cognitive testing is also a study limitation. It remains unknown how closely perceptions of distress after testing differ from those present before testing. Lastly, we recognize that our findings represent data collected from a single site. Patient populations with different characteristics and alternate clinical settings may respond differently to cognitive testing.

Overall, these results show that cognitive tasks provoke more distress in patients with mild-moderate AD compared with persons who do not have dementia, and that this distress is more closely related to patient awareness about test difficulty and performance, than actual test performance or dementia severity. Consequently, clinicians should consider the value of

monitoring patients' insight into their cognitive ability, as well as test performance, to help gauge the psychological effects of the disease. Future studies are needed to clarify the prognostic significance of distress related to testing and to determine appropriate interventions, if any, which may benefit these patients.

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References

1. Connor DJ, Salmon DP, Sandy TJ, Galasko D, Hansen LA, Thal LJ. Cognitive profiles of autopsy-confirmed Lewy body variant vs pure Alzheimer disease. Arch Neurol 1998;55:994–1000. [PubMed: 9678318]
2. Kraybill ML, Larson EB, Tsuang DW, et al. Cognitive differences in dementia patients with autopsy-verified AD, Lewy body pathology, or both. Neurology 2005;64:2069–73. [PubMed: 15985574]
3. Morris JC, Edland S, Clark C, et al. The consortium to establish a registry for Alzheimer's disease (CERAD). Part IV. Rates of cognitive change in the longitudinal assessment of probable Alzheimer's disease. Neurology 1993;43:2457–65. [PubMed: 8255439]
4. Leber, P. Guidelines for the clinical evaluation of antidementia drugs. Rockville, MD: Food and Drug Administration; 1990.
5. Sevush S, Leve N. Denial of memory deficit in Alzheimer's disease. Am J Psychiatry 1993;150:748–51. [PubMed: 8480820]
6. Vogel A, Stokholm J, Gade A, Andersen BB, Hejl AM, Waldemar G. Awareness of deficits in mild cognitive impairment and Alzheimer's disease: do MCI patients have impaired insight? Dement Geriatr Cogn Disord 2004;17:181–7. [PubMed: 14739542]
7. Tiberti C, Sabe L, Kuzis G, Garcia Cuerva A, Leiguarda R, Starkstein SE. Prevalence and correlates of the catastrophic reaction in Alzheimer's disease. Neurology 1998;50:546–8. [PubMed: 9484396]
8. Folstein MF, Folstein SE, McHugh PR. Mini-mental state. J Psychiatr Res 1975;12:189–98. [PubMed: 1202204]
9. Isaacs B, Kennie AT. The Set test as an aid to the detection of dementia in old people. Br J Psychiatry 1973;123:467–70. [PubMed: 4748864]
10. Kaplan, E.; Goodglass, H.; Weintraub, S. The Boston Naming Test. Philadelphia: Lea & Febiger; 1983.
11. Atkinson RC, Shiffrin RM. The control of short-term memory. Scientific American 1971;225:82–90. [PubMed: 5089457]
12. Wechsler, D. Wechsler Memory Scale-Revised Manual. San Antonio, Tex; Psychological Corp: 1987.
13. Morris JC, Heyman A, Mohs RC, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part I. Clinical and neuropsychological assessment of Alzheimer's disease. Neurology 1989;39:1159–65. [PubMed: 2771064]
14. Wechsler, D. Manual for the Wechsler Adult Intelligence Scale (WAIS). New York, NY: The Psychological Corporation; 1955.
15. Brink, TL. Clinical gerontology: a guide to assessment and intervention. New York: Haworth Press; 1986.
16. Clark CM, Ewbank DC. Performance of the dementia severity rating scale: a caregiver questionnaire for rating severity in Alzheimer disease. Alzheimer Dis Assoc Disord 1996;10:31–9. [PubMed: 8919494]
17. Chandler MJ, Lacritz LH, Hynan LS, et al. A total score for the CERAD neuropsychological battery. Neurology 2005;65:102–6. [PubMed: 16009893]

18. Mccullagh P. Regression-Models for Ordinal Data. Journal of the Royal Statistical Society Series B-Methodological 1980;42:109–142.

19. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA 1998;280:1690–1. [PubMed: 9832001]

20. Palmer AG, Tucker S, Warren R, Adams M. Understanding women's responses to treatment for cervical intra-epithelial neoplasia. Br J Clin Psychol 1993;32 (Pt 1):101–12. [PubMed: 8467271]

21. Karlawish JH, Casarett DJ, James BD, Xie SX, Kim SY. The ability of persons with Alzheimer disease (AD) to make a decision about taking an AD treatment. Neurology 2005;64:1514–9. [PubMed: 15883310]

22. Lupien SJ, Gaudreau S, Tchiteya BM, et al. Stress-induced declarative memory impairment in healthy elderly subjects: relationship to cortisol reactivity. J Clin Endocrinol Metab 1997;82:2070–5. [PubMed: 9215274]

23. Wilson RS, Fleischman DA, Myers RA, et al. Premorbid proneness to distress and episodic memory impairment in Alzheimer's disease. J Neurol Neurosurg Psychiatry 2004;75:191–5. [PubMed: 14742585]

24. Payne JD, Nadel L, Allen JJ, Thomas KG, Jacobs WJ. The effects of experimentally induced stress on false recognition. Memory 2002;10:1–6. [PubMed: 11747571]

25. Phelps EA, Hyder F, Blamire AM, Shulman RG. FMRI of the prefrontal cortex during overt verbal fluency. Neuroreport 1997;8:561–5. [PubMed: 9080448]

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Table 1

Demographic Characteristics and Prevalence of Distress for Patients With and Without Alzheimer's Dementia.

Patient Characteristics	Dementia n = 154	Cognitively Intact n = 62	t	df	*P*
Age (years)	77.5 ± 8	73.1 ± 9	3.22	101	.002
Female	97 (63)	43 (69)	-	1	.375*
Years of Education	13 ± 5	15 ± 4	3.11	129	.002
Race			-	2	.337*
White	114 (74)	40 (65)	-	-	-
Black	25 (16)	15 (24)	-	-	-
Multi-racial	15(4)	7 (11)	-	-	-
Ethnicity			-	1	.379†
Latino	18 (12)	10 (16)	-	-	-
Non-Latino	136 (88)	53 (84)	-	-	-
Mini-mental Status Exam	20.7 ± 4	28.8 ± 2	19.8	213	<.001
Geriatric Depression Scale	1 (0,13)	0 (0,6)	-	-	.001‡
Cognitive Test Performance					
Verbal Fluency	9 ± 4	20 ± 6	13.0	93	<.001
Boston Naming	12 ± 3	14 ± 1	10.6	210	<.001
Clock Drawing	4 ± 3	1 ± 1	10.8	209	<.001
Digit Symbol	27 ± 17	52 ± 13	11.1	147	<.001
Wordlist Memory	11 ± 5	22 ± 4	17.2	142	<.001
Wordlist Recognition	15 ± 3	20 ± 1	14.2	149	<.001
Wordlist Recall	2 ± 2	7 ± 2	20.2	116	<.001
Logical Memory 1	8 ± 6	25 ± 9	14.5	88	<.001
Logical Memory 2	2 ± 4	23 ± 9	16.2	71	<.001
Self Reported Distress, n (%)			-	3	.002*
None	46 (30)	33 (53)	-	-	-
Mild	46 (30)	18 (29)	-	-	-
Moderate	35 (23)	10 (16)	-	-	-
Severe	25 (17)	1 (2)	-	-	-
Perceived Test Performance Compared to 10 Years Ago, n (%)			-	1	.89*
Same or Better	60 (40)	25 (41)	-	-	-

Patient Characteristics	Dementia n = 154	Cognitively Intact n = 62	t	df	*P*
Worse	90 (60)	36 (59)	-	-	-
	Perceived Difficulty of Test, n (%)		-	1	.11*
Very to Somewhat Easy	76 (51)	38 (63)	-	-	-
Very to Somewhat Difficult	73 (49)	22 (37)	-	-	-

Values are express as mean ± SD, frequency (percent), or median (upper bound, lower bound)

*Pearson Chi Square

†Fisher's Exact Test

‡Wilcoxon Rank Sum Test

SD= standard deviation

Table 2

Relative Risk of Reporting Distress after Cognitive Testing in Patients with Mild-moderate Alzheimer's Disease for Demographic and Disease Factors.

	Bivariate	Multivariate*
Patient Factor	**RR (95% CI)**	
Age	0.99 (0.97–1.00)	0.98 (0.97–1.00)
Female	0.88 (0.68–1.07)	-
White	1.06 (0.85–1.21)	1.29 (1.06–1.38)†
Years of Education	1.00 (0.98–1.02)	0.97 (0.94–1.00)
Dementia Severity Scale	1.01 (0.99–1.02)	-
Geriatric Depression Scale Score	1.03 (1.00–1.06)	1.01 (0.97–1.04)
Cognitive Performance (Composite Score)	1.01 (0.99–1.03)	0.99 (0.97–1.03)
Perceived Greater Test Difficulty	1.32 (1.25–1.37)†	1.32 (1.22–1.38)†
Perceived Worse Test Performance	1.21 (1.07–1.30)†	1.25 (1.08–1.34)†

*Model adjusts for age, race, years of education, Geriatric Depression Scale score, cognitive performance, perceived test difficulty, and perceived test performance.

†Statistically significant at P< .02

Table 3

Relative Risk of Reporting Distress after Cognitive Testing in Patients with Mild-Moderate Alzheimer's Disease Based on Cognitive Test Performance.

Model	Cognitive Domain	Bivariate	Multivariate*
		RR (95% CI)	
1	Language	0. 95 (0.89–0.99)†	0.90 (0.83–0.96)‡
2	Memory	1.00 (0.98–1.03)	0.98 (0.89–1.08)
3	Processing Speed	0.95 (0.84–1.04)	0.76 (0.49–1.20)
4	Visual Spatial Ability	0.96 (0.87–1.05)	0.93 (0.66–1.34)

*Model 1 adjusts for age, race, gender, years of education, and geriatric depression scale scores; models 2, 3, and 4 adjust for age, race, gender, years of education, geriatric depression scale scores, and dementia severity.

†Statistically significant at P< .04

‡Statistically significant at P< .002