Is Functional Decline Necessary for a Diagnosis of Alzheimer's disease?

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1. Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder that results in multiple cognitive deficits, which, by definition, include memory impairment and at least one second domain (attention, language, visual perception, praxis, orientation or frontal executive ability). In addition to progressive cognitive deterioration, patients with AD may also experience declines in the ability to perform activities of daily living (ADL).[1] Daily functional impairment measured by ADL is required by some diagnostic criteria for AD (DSM-IVcriteria[2]), but not by others (NINCDS-ADRDA criteria[1]). In the early stages of AD, performance of daily functional activities essential to maintaining independence (instrumental activities of daily living (IADL)) may be altered.[3, 4] In later stages, there is a progressive decline in basic activities involving physical self-care (ADL).[4, 5]

A Recent study using comprehensive clinical evaluations and detailed neuropsychological measures with accurate information from the caregiver demonstrated that very mild AD patients can be detected in the preclinical stages, even without definite functional impairment.[6] However, these patients are often classified as Mild Cognitive Impairment (MCI) and not AD, with implications for treatment, since there are currently no therapies approved to treat MCI. Other authors suggest that the absence of ADL impairment is consistent with preclinical AD or MCI.[7,8] Although general aspects of the functional status of elderly patients with AD is relatively well-known, it is not clear whether mild AD patients with functional impairment really differ from those without functional impairment at baseline or with respect to annual change on psychometric measures.

The purpose of this study is to determine whether baseline characteristics or annual change scores on psychometric measures differ between mild AD patients who have measurable functional impairment at baseline versus those who do not. Similar annual change on these measures could support the theory that functional decline represents advancement of the AD process, and should not be a required feature of diagnosis.

2. Patients and Methods

Patients

We recruited probable AD patients in the Baylor Alzheimer's Disease and Memory Disorders Center between 1989 and 2005.[9] All patients with at least one annual follow-up evaluation and mild AD(MMSE[10] ≥20) were eligible (n=413).

Methods

Duration of symptoms (physician's estimate of duration) was estimated according to a previously published method.[11] The ADL scales described by Lawton and Brody[12] were used. These measures, initially developed for use in the general geriatric population, consist of the Physical Self-Maintenance Scale (PSMS) and the instrumental ADL (IADL). The PSMS is a six-item scale that assesses the subject's ability to perform tasks of physical self-care. Each item is scored from 1 (no impairment) to 5 (severe impairment) based on an interview with the caregiver. The maximum total score is 30 but a score of 6 indicates normal basic ADL. The IADL consist of eight items that address the individual's ability to function independently. Severity is scored from 1 for no impairment to 3 on three items, 4 on three items and 5 on the remaining two items. The maximum score of IADL is 31 and a score of 8 indicates normal complex ADL. A score of zero was sometimes given for three items (food preparation, housekeeping, laundry), which were found to have gender bias in Lawton and Brody's initial reliability and validity study.[12] A zero was given whenever the rater decided that the item could not be assessed, because the patient did not perform the activity in question prior to the onset of the disease. We defined abnormal ADL status as: total scores on the PSMS >6 and total scores on the IADL >9. We excluded from the analysis any subjects who scored a zero on an IADL question except when all of the subscore were = 1 and the total score would have been normal even is the zero item had been scored as 1 (n=29). Of the 384 eligible subjects, we excluded subjects who were missing any part of the comprehensive neuropsychological assessment, PSMS or IADL scores (n=117). Based on their initial ADL scales the final group (n=267) was divided into two groups: unimpaired ADL (n=40) and impaired ADL (n=227) using scores on the PSMS and IADL.[12]

Statistical analysis

Descriptive statistics (i.e., frequencies for categorical variables, means and SDs for continuous variables) for the following variables were initially determined for the groups as a whole: sex, ethnicity, age, education, physician's estimate of symptom duration, initial-visit MMSE score, ADAS-cog[13], PSMS, IADL, ADL status, 1-year follow-up MMSE score, ADAS-cog, PSMS, IADL, ADL status.

The characteristics of persons with normal versus impaired functional status at baseline were compared with an analysis of variance (ANOVA) for continuous variables and chi-square test for categorical variables. The differences in scores on cognitive and functional measures from baseline to the first follow-up visit were also compared by ANOVA.

3. Results

Forty patients (15%) were unimpaired in ADL at baseline and 227 (85%) were impaired. The two groups did not differ for sex, age, education, or ethnicity. (Table 1) However, the group with unimpaired ADL at baseline had significantly shorter symptom duration (p=0.010) and slightly better baseline test scores versus those with impaired ADL. (Table 2)

The psychometric scores of each group (unimpaired ADL versus impaired ADL) at baseline and year 1 shown are in Table 2. Annual psychometric change was numerically smaller for the initially unimpaired group in all measures, but both groups on every measure worsened by a small amount. Only the PSMS annual change was significantly different, with changes greater in the group that had impaired IADL at baseline (p=0.032). (Table 2)

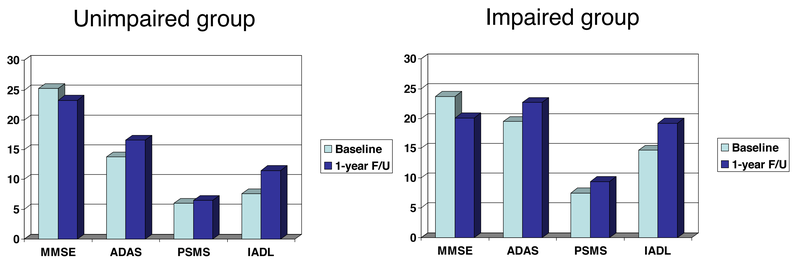
After 1 year, 56% of the initially unimpaired group and 6% of the initially impaired group had no reported PSMS/IADL impairment (McNemar's Chi-square = 0.065).

Table 1. Demographic data in early Alzheimer's disease patients

Variable		Baseline ADL status		p
		Unimpaired group	Impaired group	
Age, years	N	40	227	
	Mean (SD)	71.5 (7.93)	74.0 (7.93)	0.074
Education, years	N	39	226	
	Mean (SD)	14.2 (3.23)	14.5 (6.48)	0.744
Duration of symptom, years	N	40	227	
	Mean (SD)	2.6 (1.19)	3.6 (2.34)	0.01
Female, %	N (%)	40 (82.5)	227 (71.4)	0.999
Race/ ethnicity, %	N (%)	40 (100)	227 (100)	0.210
White	N (%)	35 (87.5)	207 (91.2))	-
Black	N (%)	2 (5.0)	9 (4.0)	-
Hispanic	N (%)	1 (2.5)	6 (2.6)	-
Other	N (%)	2 (5.0)	5 (2.2)	-

Table 2. Test results of initial and 1-year follow-up assessment in early Alzheimer's disease patients

Variable		Unimpaired group			Impaired group			p
		Baseline	1-year F/U	Differences	Baseline	1-year F/U	Differences	
MMSE	N	40	37	-	225	206	-	
	Mean (SD)	25.3 (2.43)	23.3 (4.42)	2.0 (4.85)	23.7 (2.66)	20.1 (5.40)	3.6 (4.70)	0.061
ADAS	N	39	37	-	218	198	-	
	Mean (SD)	13.8 (4.63)	16.6 (7.86)	2.6 (6.40)	19.5 (7.80)	22.7 (10.99)	3.7 (8.62)	0.463
PSMS	N	40	39	-	227	219	-	
	Mean (SD)	6.0 (0.00)	6.5 (1.14)	0.5 (1.14)	7.5 (2.14)	9.4 (4.57)	1.8 (3.84)	0.032
IADL	N	40	39	-	227	218	-	
	Mean (SD)	7.6 (1.32)	11.5 (4.86)	3.6 (4.79)	14.7 (5.07)	19.2 (6.36)	4.4 (5.40)	0.396



4. Discussion

The results of the current study demonstrate that the clinical diagnosis of AD can be made on the basis of impairment memory and a second cognitive domain, but in the absence of impaired ADL. The AD patients in both groups had comparable rate of annual change on cognitive (MMSE, ADAScog) and functional (PSMS/IADL) measures over one year. Only the change from baseline in PSMS differed between the groups. Since it is well-documented that basic ADL impairment usually follows complex ADL impairment chronologically, thus the finding is not unexpected.

The fact that the psychometric scores of the unimpaired group were better than those of the impaired group at baseline suggest that the presence of ADL impairment, in addition to 2 cognitive domains, is a marker of more advanced disease. This interpretation is supported by the fact that duration of disease since first symptoms was significantly shorter for the group with no ADL impairment at baseline.

A limitation of the current study is the fact that our population is relatively well-educated, although mean education did not differ between the groups. The significance of ADL impairment at baseline might be associated with more pronounced annual change difference in a less educated group. The fact that our patients included a wide range of formal years of education (6–20 years) mitigates this concern to some extent.

Finally, our group of AD patients without ADL impairment at baseline was quite small. It is likely that with a larger sample size, some of the annual change scores would have differed significantly between the initially impaired and initially unimpaired groups. In fact, since baseline scores are correlated with annual change scores on most measures, we would expect this. However, the direction of change, as well as the magnitude of annual change in both groups supports the hypothesis that both represent mild AD, uncontaminated by static conditions. The DSM IV criteria[2], which require functional decline in order to diagnose AD, likely lead to at least a one year delay in diagnosis for approximately 15% of AD cases. Given the implications for treatment and eligibility for other support services, this delay may be both unwarranted and undesirable.

REFERENCES

1. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology. 1984;34:939-944
2. Association AP. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC: American Psychiatric Association. 1993
3. Stern Y, Hesdorffer D, Sano M, Mayeux R. Measurement and prediction of functional capacity in Alzheimer's disease. Neurology. 1990;40:8-14
4. Green CR, Mohs RC, Schmeidler J, Aryan M, Davis KL. Functional decline in Alzheimer's disease: a longitudinal study. J Am Geriatr Soc. 1993;41:654-661
5. Gauthier S, Gelinas I, Gauthier L. Functional disability in Alzheimer's disease. Int Psychogeriatr. 1997;9 Suppl 1:163-165
6. Salmon DP, Thomas RG, Pay MM, Booth A, Hofstetter CR, Thal LJ et al. Alzheimer's disease can be accurately diagnosed in very mildly impaired individuals. Neurology. 2002;59:1022-1028
7. Morris JC, Storandt M, Miller JP, McKeel DW, Price JL, Rubin EH et al. Mild cognitive impairment represents early-stage Alzheimer disease. Arch Neurol. 2001;58:397-405
8. Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2001;56:1133-1142
9. Doody R, Pavlik V, Massman P, Kenan M, Yeh S, Powell S et al. Changing patient characteristics and survival experience in an Alzheimer's center patient cohort. Dement Geriatr Cogn Disord. 2005;20:198-208
10. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12:189-198
11. Doody RS, Dunn JK, Huang E, Azher S, Kataki M. A method for estimating duration of illness in Alzheimer's disease. Dement Geriatr Cogn Disord. 2004;17:1-4
12. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist. 1969;9:179-186
13. Rosen WG, Mohs RC, Davis KL. A new rating scale for Alzheimer's disease. Am J Psychiatry. 1984;141:1356-1364