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 other domain compromised. 

2. Patients and Methods

Methods
Duration of symptoms (physician’s estimate of duration) was estimated according to a previously published method.4 The ADL scores described in Table 1 were derived from these measures, including the Katz Functional Status Instrument, which is a widely validated measure for use in the general population. The Katz Functional Status Instrument was conducted by trained clinicians. Each item is scored from 1 (no impairment) to 5 (severe impairment) based on an interview with the caregiver. The maximum total score is 18 but scores of 6 indicates normal. The Katz ADL status is divided into two groups: unimpaired ADL (n=40) and impaired ADL (n=227). 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 status impairment at baseline and those with unimpaired functional status at baseline or with respect to annual change on psychometric measures.

Statistical analysis
Differences of variables (frequencies for categorical variables, means and SDs for continuous variables) for the following variables were analyzed using general linear models (GLM) with age, sex, and education as covariates. The chi-square test was used for differences between categorical variables. The Student’s t-test was used for differences between continuous variables.

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, or ethnicity. At year 1 shown in Table 1, annual psychometric change was numerically smaller for the initially impaired 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 ADL 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 = 0.085.

4. Discussion

The results of the current study demonstrate that the clinical diagnosis of AD can be made on the basis of impairment in 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, ADAS-cog) and functional (PSMS/IADL) measures over one year. Only the change from baseline in PSMS IADL differed between the groups. Since it is well-documented that basic ADL impairment usually follows complex ADL impairment chronologically, the finding is not unexpected.

The fact that the psychometric scores of the impaired 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 finding 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 that the fact our population is relatively well-educated, although mean education did not differ between the groups.

Finally, our group of AD patients without ADL impairment at baseline was quite pronounced annual change difference in a less educated group. The fact that differences in direction of change, as well as the magnitude of annual change in both groups 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, unaccompanied by static conditions. The DSM IV criteria, 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. Alzheimer’s Association. Alzheimer’s Disease and Memory Disorders Center Located in the Baylor College of Medicine. Houston, TX, USA. Contact e-mail: ndoody@bcm.tmc.edu