Change in Cognitive Function in Older Persons From a Community Population

Relation to Age and Alzheimer Disease

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Objective: To examine change in cognitive function in older persons sampled from a community population, and its relation to age and Alzheimer disease.

Design: Prospective cohort study with an average of 3.5 years of follow-up.

Setting: East Boston, Mass—a geographically defined, urban, working-class community.

Participants: A stratified, random sample of persons 65 years and older underwent uniform, structured clinical evaluation for Alzheimer disease. The 388 persons (89.2% of those eligible) who completed at least 1 annual follow-up evaluation were studied: 97 had Alzheimer disease at baseline; 95 developed Alzheimer disease during the study; and 196 were unaffected.

Outcome Measures: Eight cognitive performance tests were administered, then converted to population-weighted z scores and averaged to create a composite summary measure of cognitive function. Initial level of and change in this score were the outcome measures.

Results: In the population as a whole, many persons experienced a decline in cognitive performance, and age was related to both initial level and rate of decline. Analyses were conducted in 3 subgroups: persons with Alzheimer disease at baseline, those who developed Alzheimer disease during the study, and those who remained unaffected. In both Alzheimer disease subgroups, substantial cognitive decline was observed, but neither initial level nor rate of decline was related to age. In unaffected persons, little cognitive decline was evident, and there was a small, inverse association of age with initial level of cognitive function.

Conclusion: In a general population sample, there was little evidence of cognitive decline during a 3.5-year period among persons who remained free of Alzheimer disease.

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In longitudinal, population-based studies of persons 65 years and older, advancing age is associated with more rapid cognitive decline and with increased prevalence and incidence of Alzheimer disease. It is likely that some of the cognitive decline observed in aged populations reflects Alzheimer disease. Unfortunately, few longitudinal, population-based studies include clinical evaluation for dementia and Alzheimer disease.

Knowledge of the relations among cognitive function, age, and Alzheimer disease comes mainly from studies of persons who are evaluated in clinical settings, but these studies are subject to bias for several reasons. First, a minority of all persons with Alzheimer disease come to medical attention. Therefore, clinical settings are unlikely to represent the full spectrum of Alzheimer disease in the general population. Second, many factors influence who seeks medical attention; in general, persons evaluated in clinical settings are more likely to be male, younger, and have more years of formal education than those with Alzheimer disease in the general population. Third, it is difficult to identify comparable persons without Alzheimer disease in clinical studies. Furthermore, follow-up participation in published longitudinal studies is often low or cannot be determined; this may lead to bias because persons who return for follow-up evaluation may differ from those who do not.

In the present study, a stratified random sample of persons from a defined community population underwent uniform structured evaluations that included clinical classification for Alzheimer disease and cognitive function testing. Evaluations were repeated annually for an
METHODS

OVERVIEW OF STUDY DESIGN

From January 1982 to December 1983, the urban community of East Boston, Mass, was censused, and all persons 65 years and older were asked to participate in an interview that included brief tests of memory and cognition. Of those eligible, 80.7% (362/4483) were interviewed and had cognition tested. A random sample of 714 persons, stratified by age, sex, and level of memory performance, was identified for detailed clinical evaluation. Of these 714 persons, 54 died before being asked to participate, 467 (70.8% of survivors) underwent clinical evaluation, and 193 declined participation. Further details of the study design and sampling plan are published elsewhere.17

BASELINE EVALUATION

Diagnostic Classification

Structured clinical evaluation of the 467 persons took place an average of 16.3 months after the population interview. Evaluation included a medical history, neurologic examination, cognitive testing, brief psychiatric evaluation, informant interview, laboratory evaluation, and computed tomography of the brain in a subset. Diagnosis of Alzheimer disease was based on National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer’s Disease and Related Disorders Association (NINCDS/ADRA)16 criteria, which require a history of cognitive decline and evidence of impaired memory and cognition on examination. Other neurologic and psychiatric conditions judged to contribute to cognitive impairment were also recorded.

Cognitive Function Testing

Eight tests (Table 1) were administered to help inform clinical classification and provide a baseline for measuring change: immediate and delayed recall of a brief story; a spatial working memory task requiring identification of successive additions to a previously viewed stimulus array; naming 15 pictured and 5 actual objects; reading 2 brief phrases; copying simple designs; discriminating geometric figures in a match-to-sample format; and identifying similarities and differences among sets of visually presented stimuli. Additional psychometric information on these tests is reported elsewhere.17,18,20

RESULTS

Of the 467 persons who completed the baseline clinical evaluation, 32 died before the first follow-up evaluation and 388 completed at least 1 follow-up evaluation from which a summary cognitive score could be computed. Analyses were based on these 388 persons (89.2% of those eligible) who completed an average of 4.5 examinations (range, 2-6), 93.1% of those scheduled, during an average interval of 3.5 years.

At baseline evaluation, 97 persons met NINCDS/ADRA criteria for Alzheimer disease. Because the stratified sampling plan oversampled people with cognitive impairment, a substantial proportion developed Alzheimer disease during follow-up; 95 persons who did not meet criteria for Alzheimer disease at baseline did so on 1 or
more follow-up examinations (40, 24, 13, 15, and 3 on evaluations 2-6, respectively). The remaining 196 persons never met the diagnostic criteria. Table 2 provides descriptive information on the subgroups, weighted to the community population. In comparison to unaffected persons, those with Alzheimer disease were older and less educated, and had lower scores at baseline on the summary measure of cognitive function. Follow-up participation was similar in the subgroups.

In an initial analysis of the entire population sample (Table 3), the summary cognitive score declined by an average of 0.039 standard score units per year (95% confidence interval [CI], −0.024 to −0.053). This was compatible with the estimate that the average cognitive score in the entire population was 0.050 standard score units (95% CI, −0.039 to −0.050) lower at baseline for each year of age. On average, cognitive score also declined more rapidly for older persons in the entire population. The estimate of the interaction between baseline age and annual change during the study was −0.004 (95% CI, −0.002 to −0.005)—approximately one tenth the size of the term representing annual change, indicating that cognitive score declined approximately 10% faster for each year older a person was at baseline.

Figure 1 shows the estimates of change in cognitive function from this model for each person in the population sample. The slope of each line is a smoothed estimate from all measurements of summary score for that person. Figure 1 is organized according to age of each person at baseline, and the length of each line corresponds to the number of years of observation for that individual. Although the overall trend of cognitive decline with advancing age is evident, there is much heterogeneity; some persons decline sharply, many not at all, and others seem to improve. This variability is not easily accounted for by a simple homogeneous aging process. Moreover, the people who start at lower levels of function appear in Figure 1 to be declining faster; this is confirmed by a significant positive correlation between the person-specific initial levels of cognitive performance or on rate of decline in performance and person-specific slopes (r = 0.36, P <.001).

To examine the contribution of Alzheimer disease to cognitive decline in this community population, analyses were performed for 3 subgroups: persons with Alzheimer disease at baseline, those who developed Alzheimer disease during follow-up, and those who remained unaffected (Table 4). As expected, persons with Alzheimer disease at baseline experienced the largest declines in cognitive function—an average summary cognitive score decline of 0.097 standard score units per year (95% CI, −0.046 to −0.147). Average decline among those without Alzheimer disease at baseline but who developed it during the study was somewhat less: 0.055 standard score units per year (95% CI, −0.022 to −0.088). There was no strong effect of age on baseline level of cognitive performance or on rate of decline in performance.
for either Alzheimer disease subgroup. The pattern in those who remained free of Alzheimer disease throughout the study was substantially different: their cognitive performance remained stable, with an estimated average annual change of 0.004 standard score units per year (95% CI, −0.017 to 0.025). Baseline level of cognitive function was lower by 0.017 standard score units (95% CI, −0.007 to −0.027) per year of age on average, but there was no evidence that cognitive performance declined more rapidly during the study among older unaffected persons.

Figure 2 shows the estimates of change in cognitive performance for persons within diagnostic subgroups. Substantial cognitive decline is evident in persons with Alzheimer disease diagnosed at baseline (Figure 2, A) or during follow-up (Figure 2, B). On average, the rate of decline appears more rapid in the former than in the latter subgroup, although much variability among persons is seen in both. In contrast, little cognitive decline is evident in the unaffected subgroup (Figure 2, C). Within each subgroup, age appears unrelated to change in cognitive function.

Secondary analyses addressed 3 potentially confounding factors. First, because level of education is related to age and cognitive test performance and differed in persons with and without Alzheimer disease, analyses were repeated with terms for education and its interaction with years elapsed during the study. Second, other neurologic and psychiatric conditions judged to impair cognition were noted on baseline and follow-up evaluations; these conditions were depression (n = 23), stroke (n = 14), alcoholism (n = 6), Parkinson disease (n = 5), psychosis (n = 5), retardation (n = 2), and subacute combined degeneration (n = 2). Analyses were repeated with these 57 persons excluded. Third, to see if results depended on how the summary measure was formed, analyses were also repeated using the total items correct on the 8 tests instead of the z score measure. Results from these secondary analyses (data not shown) were consistent with those from primary analyses: in the entire population sample, decline occurred and was related to age; in those with Alzheimer disease, decline occurred but was unrelated to age; and in those unaffected, decline did not occur.

Overall, this community population experienced a measurable decline in cognitive performance during 3.5 years. Dividing the population into diagnostic subgroups, however, demonstrated that substantial cognitive decline was almost completely restricted to persons either who had

### Table 4. Change in the Summary Measure of Cognitive Function Among 3 Diagnostic Subgroups of the Population Sample*

<table>
<thead>
<tr>
<th>Diagnostic Subgroup</th>
<th>Coefficient</th>
<th>SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer disease at baseline</td>
<td>−0.097</td>
<td>0.026</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Annual change during study</td>
<td>−0.020</td>
<td>0.011</td>
<td>.07</td>
</tr>
<tr>
<td>Age at baseline, y</td>
<td>−0.003</td>
<td>0.004</td>
<td>.47</td>
</tr>
<tr>
<td>Interaction between baseline age and annual change</td>
<td>−0.003</td>
<td>0.004</td>
<td>.47</td>
</tr>
<tr>
<td>Met criteria for Alzheimer disease during follow-up</td>
<td>−0.055</td>
<td>0.017</td>
<td>.001</td>
</tr>
<tr>
<td>Annual change during study</td>
<td>−0.004</td>
<td>0.010</td>
<td>.71</td>
</tr>
<tr>
<td>Age at baseline, y</td>
<td>−0.002</td>
<td>0.003</td>
<td>.36</td>
</tr>
<tr>
<td>Interaction between baseline age and annual change</td>
<td>−0.002</td>
<td>0.003</td>
<td>.36</td>
</tr>
<tr>
<td>Unaffected</td>
<td>0.004</td>
<td>0.011</td>
<td>.68</td>
</tr>
<tr>
<td>Annual change during study</td>
<td>−0.017</td>
<td>0.005</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age at baseline, y</td>
<td>0.000</td>
<td>0.001</td>
<td>.74</td>
</tr>
</tbody>
</table>

*Values are from random-effects regression models and are weighted to reflect sampling probabilities.
Alzheimer disease diagnosed at the baseline evaluation or who met criteria for the disease during follow-up. During this period, there was little evidence of cognitive decline with advancing age among persons who remained unaffected by the disease.

Occurrence of cognitive decline among older persons is well documented, with recent longitudinal, population-based studies providing the most direct evidence. There are few longitudinal studies, however, of the change in cognitive performance among persons who have undergone clinical evaluation and been found to be without dementia or Alzheimer disease. The results of several case-control studies and one population-based study suggest there is little to no cognitive decline in persons without clinical evidence of dementia or Alzheimer disease during study intervals ranging from about 1 to 5 years.

Study data are also relevant to characterizing the course of Alzheimer disease in the general population. Persons diagnosed as having Alzheimer disease at baseline began the study with a summary cognitive score more than one standard score unit below unaffected persons and declined an average of about one tenth of a unit per year. Persons who developed the disease during follow-up began the study with an average cognitive score of about one half of a standard score unit below that of unaffected persons, and declined an average of about one twentieth of a unit annually. The evidence of substantial cognitive impairment in this subgroup at baseline—before a clinical diagnosis of Alzheimer disease was made—reinforces the view that gradual cognitive decline typically precedes the onset of clinically manifest dementia in this disease. That the rate of cognitive decline was more rapid in persons with baseline Alzheimer disease compared with this group suggests a gradually accelerating rate of decline during the disease course.

The relation of age to cognitive decline among persons with Alzheimer disease has not been examined in longitudinal, population-based studies, and studies of clinical samples yielded mixed results. Younger age was associated with more rapid cognitive decline in some studies, but others found the opposite association, mixed results, or no association. Among persons with Alzheimer disease in this population, age was unrelated to change in cognitive function and only marginally related to initial level. It should be emphasized that persons younger than 65 years in this population were not sampled by this study, and questions regarding Alzheimer disease before this age were not addressed.

Several methodologic features of this study increase the likelihood that the results are valid. First, participants represented a random sample of persons with and without Alzheimer disease from a geographically defined community population. All persons 65 years and older within the community were eligible, and rates of participation were high, reducing the likelihood of bias from nonrandom initial participation. Second, the rate of participation in the follow-up evaluation was high, and similar for affected and unaffected persons, reducing the likelihood of bias from nonrandom follow-up participation. Third, cognitive function was expressed as a composite of 8 individual performance tests of varying difficulty levels. Use of a composite measure extends the range within which individual differences can be detected, thereby reducing bias from floor or ceiling effects encountered in previous studies. Fourth, high follow-up participation, with an average of 4.5 evenly spaced data collection points and a cognitive measure with minimal floor and ceiling effects, permitted the use of statistical models to characterize person-specific paths of change in cognitive function. This reduced the likelihood of bias from regression to the mean and from inadequate ability to describe within-person correlations.

Our study has important limitations. Implementation criteria for the clinical diagnosis of Alzheimer disease can vary among studies because disease onset is typically by minute degrees over a period of time, and different investigators using the same criteria can place the cut point between normality and disease at different places along this continuum. The approach taken in this study—use of uniform structured evaluation, prior specification of diagnostic criteria, and blinding of evaluators at each annual evaluation to previous data—reduces both individual variation within the study and bias in applying these criteria. Nonetheless, the degree to which substantial cognitive decline is largely restricted to persons who had Alzheimer disease at baseline and to those who developed the disease during the study will depend on the placement of the diagnostic cut point between normality and Alzheimer disease. If criteria that restricted the diagnosis of Alzheimer disease to persons with more severe disease had been used, it is likely that this finding would not have been as strong. Because participants were followed closely with annual clinical evaluations, the study was especially efficient in detecting persons who met the criteria for a diagnosis of Alzheimer disease during follow-up. It is likely that longitudinal clinicopathologic studies will provide the most direct evidence of the contribution of Alzheimer disease to age-related cognitive decline.

Our finding of little or no cognitive decline among older persons who are free of Alzheimer disease is consistent with those of the few previous studies that have used diagnostic criteria to distinguish a group free of the disease. Different results might have been obtained with specific (or different global) measures of cognitive function, or with a longer observation period. The results, however, argue against the existence of substantial cognitive decline that would be evident during a period of a few years from advancing age alone.

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REFERENCES


