Association of Subjective Memory Complaints With Subsequent Cognitive Decline in Community-Dwelling Elderly Individuals With Baseline Cognitive Impairment

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Objective: The validity of subjective memory complaints has been questioned by clinical studies that have shown little relationship between memory complaints and objective memory performance. These studies often have been cross-sectional in design, have excluded individuals with cognitive impairment, or have lacked a comparison group. The authors conducted a study that attempted to avoid these limitations. Method: Memory complaints of 364 nondemented, community-dwelling elderly individuals were recorded as present or absent at the baseline evaluation. After 1 year, 169 subjects were reevaluated. Standardized neurologic and neuropsychological evaluations were used at each assessment to classify subjects as normal or cognitively impaired. Results: At baseline, 31% of the normal subjects and 47% of those with cognitive impairment had memory complaints. Subjects with memory complaints had higher Hamilton depression scale scores than subjects without memory complaints but equivalent scores on a measure of total recall. At follow-up, multivariate analyses showed that subjects with baseline memory complaints had significantly greater decline in memory and cognition than subjects without memory complaints. Secondary analyses showed this effect to be confined to subjects with baseline cognitive impairment. Conclusions: Memory complaints may lack validity in subjects with normal cognition, but in nondemented individuals with cognitive impairment, memory complaints may predict subsequent cognitive decline.

Numerous studies have sought to evaluate the relationship between self-reported memory complaints and memory performance in elderly populations (1–14). The results have been mixed—some studies have demonstrated a weak association (1, 2, 6, 9, 10, 14), while others have not (5, 7, 12, 13)—and the validity of the self-reported memory problems themselves has been questioned. However, many of these studies have been clinic-based or cross-sectional in design and have not included subjects with cognitive impairment or comparison subjects without memory complaints. We investigated the relationship between memory complaints and cognitive performance among elderly participants of a population-based longitudinal study. In our study, in contrast with many others, not all subjects had memory complaints, some had cognitive impairment, and a proportion of subjects were evaluated twice.

Method

Subjects

Subjects for the current study comprised a subset of subjects in a registry that had been created for the study of aging and neurological conditions in New York City (15). To establish the registry, nursing homes, home health care agencies, private practitioners, and hospital admission and discharge lists were canvassed to identify individuals with possible cognitive impairment. These individuals were then invited to complete a cognitive screening questionnaire (16) that had been modified from the Comprehensive Assessment and Referral Interview (17). Scores on this screening questionnaire could range from 0 to 15, with scores above 2 indicative of possible impairment.
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To provide a comparison group, subjects without suspected cognitive impairment from the same community were also invited to take the screening questionnaire and to participate in subsequent phases of the evaluation. After complete description of the study, written informed consent was obtained from all enrolled subjects. All subjects who scored above 2 on the screening questionnaire were referred to a clinical evaluation team as were approximately 25% of those with scores of 2 or less (indicating no impairment), who were selected at random. The evaluators were blind to the subjects’ score on the screening questionnaire. Subjects who entered this phase of the study underwent annual follow-up evaluations for up to 5 years. Baseline and follow-up evaluations were reviewed similarly. Criteria from the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association (31) were used for the diagnosis of probable or possible Alzheimer’s disease.

All neuropsychological test data were used to diagnose impairment or dementia according to the paradigm just described. For analyses of memory performance in this study we chose score on the total recall component of the Buschke Selective Reminding Test (22) as our best single objective measure. In a previous study we showed this measure to be highly sensitive to the earliest changes of Alzheimer’s disease (32).

The 17-item Hamilton depression scale (33) was administered by trained interviewers at the time of the neuropsychological battery. The goal was to administer the Hamilton depression scale to all participating subjects, but some subjects did not complete it because of limited availability of interviewers.

Statistical Analysis

At baseline, we used chi-square or two-tailed t tests to look for group differences between normal and impaired subjects with respect to demographic characteristics, frequency of memory complaints, and affective and functional status. We used analysis of covariance (ANCOVA) to compare the mean total recall score at baseline of subjects with memory complaints to that of subjects without memory complaints after we controlled for age and education.

For the follow-up analyses, we used data from baseline and 1-year follow-up evaluations to investigate whether baseline memory complaints predicted 1) decline in score on the total recall component of the Buschke Selective Reminding Test from baseline to follow-up or 2) cognitive decline, defined as a change from normal at baseline to impaired or demented at follow-up or from impaired at baseline to demented at follow-up. To evaluate whether memory complaints were associated with a decline in total recall, we performed ANCOVAs with total recall at follow-up as the dependent variable and baseline memory complaints as the independent variable of interest, after adjusting for baseline total recall, age (continuous variable), education (continuous variable), and cognitive category (normal or impaired). To investigate whether memory complaints at baseline predicted cognitive decline, we performed logistic regression analyses after adjusting for the same covariates. These analyses were repeated within separate subject groups that were stratified by education and cognitive category. Finally, logistic models were constructed with dementia as the outcome of interest to assess whether cognitive category and memory complaints were independent predictors of dementia at follow-up.

RESULTS

Baseline

The baseline evaluation was completed by 513 nondemented subjects. We excluded from our analyses 121 subjects for whom informants had contributed some history at the baseline evaluation and 28 subjects who had not been assigned a cognitive category at baseline. The excluded subjects were older and performed more poorly on memory tests than the 364 subjects that were included in this study but did not differ in gender or the proportion tested in English. The 364 study subjects consisted of 131...
subjects who were normal and 233 with cognitive impairment. The subjects with cognitive impairment were older and less educated, had higher Hamilton depression scale scores, and were more likely to have memory complaints than normal subjects (table 1).

We used ANCOVA to compare the total recall scores at baseline of subjects with memory complaints to those of subjects without memory complaints after controlling for age and years of education. The adjusted mean baseline score on the total recall component was no different for subjects with memory complaints than that for subjects without memory complaints for the total group (F=1.67, df=1, 354, p=0.20) or when analyses were conducted separately for the normal (F=2.34, df=1, 126, p=0.13) or impaired (F=0.88, df=1, 224, p=0.35) subgroups. However, in an ANCOVA adjusted for age and education that included both normal and cognitively impaired subjects, those with memory complaints had an adjusted mean score on the Hamilton depression scale that was 3.4 points higher than those without memory complaints (F=24.4, df=1, 228, p<0.0001).

Follow-Up

Of the 364 subjects that we evaluated at baseline, 169 completed a follow-up examination 1 year later. Ninety-five subjects who had completed a baseline evaluation toward the end of the enrollment period were not followed because of a change in research priorities, which required preferential evaluation of randomly selected subjects for new longitudinal studies. Forty-two subjects were not due for follow-up at the termination of the study. Other reasons for lack of follow-up included death (N=14), subject refusal (N=20), or inability to locate subject (N=20). Four subjects had incomplete evaluations. There were no significant differences between subjects who completed a follow-up evaluation and those who did not with respect to gender, age, education, proportion tested in English, prevalence of memory complaints, or scores on the Schwab and England Activities of Daily Living Scale (20), From the Buschke Selective Reminding Test (22). From the Blessed Information and Concentration Test, short version (18).

Other analyses, not shown in table 2, showed that cognitive impairment at baseline was strongly associated with dementia at follow-up (χ²=13.5, df=1, p<0.001). Because of this, and to assess the significance of baseline memory complaints for follow-up cognition independent of cognitive category, we included cognitive category as an independent variable in multivariate analyses.

An ANCOVA with total recall at follow-up as the dependent variable that compared subjects with memory complaints to those without (after covarying for baseline total recall, age, education, and cognitive category) showed significant group effects for memory complaints (F=8.1, df=1, 160, p=0.005) and cognitive category (F=4.8, df=1, 160, p=0.03). The adjusted mean score of subjects with memory complaints on total recall at follow-up was 3.0 points lower than that of subjects without memory complaints, and the adjusted mean score of subjects with impairment at baseline on total recall at follow-up was 3.0 points lower than that of normal subjects. In a separate ANCOVA that treated memory complaints as a separate main effect and included the interaction of memory complaints by cognitive category, the interaction term was significant (F=4.3, df=1, 159, p=0.04). We therefore repeated the ANCOVA separately within each baseline cognitive category. Among normal subjects, there was no difference in the adjusted mean

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Cognitive Impairment (N=131)</th>
<th>Cognitive Impairment (N=233)</th>
<th>Total (N=364)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
</tr>
<tr>
<td>Primary language English</td>
<td>71 54</td>
<td>120 51</td>
<td>191 52</td>
</tr>
<tr>
<td>Memory complaints</td>
<td>41 31</td>
<td>109* 47</td>
<td>150 41</td>
</tr>
<tr>
<td>Age (years)</td>
<td>74.2 6.6</td>
<td>77.0** 7.0</td>
<td>75.9 7.0</td>
</tr>
<tr>
<td>Education (years)</td>
<td>9.5 3.9</td>
<td>7.0** 4.0</td>
<td>7.9 4.1</td>
</tr>
<tr>
<td>Hamilton depression scale score</td>
<td>3.9 3.9</td>
<td>6.3 5.9</td>
<td>5.4 5.4</td>
</tr>
<tr>
<td>Orientation-memory-concentration</td>
<td>3.0 3.0</td>
<td>6.9** 4.8</td>
<td>5.5 4.6</td>
</tr>
<tr>
<td>Functional assessment</td>
<td>85.0 18.0</td>
<td>77.0** 21.0</td>
<td>80.0 20.0</td>
</tr>
<tr>
<td>Total recall</td>
<td>42.0 7.4</td>
<td>31.5** 7.0</td>
<td>35.3 8.8</td>
</tr>
</tbody>
</table>

*aTotal N=233 (88 subjects without and 145 subjects with cognitive impairment).
*bFrom the Blessed Information and Concentration Test, short version (18).
*cFrom the Schwab and England Activities of Daily Living Scale (20).
*dFrom the Buschke Selective Reminding Test (22).
*p<0.01. **p<0.001.
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TABLE 2. Baseline Demographic and Clinical Characteristics of Community-Dwelling Elderly Individuals Who Were Followed Up at 1 Year, by Memory Complaints at Baseline

<table>
<thead>
<tr>
<th>Variable</th>
<th>N Memory Complaints at Baseline (N=99)</th>
<th>Memory Complaints at Baseline (N=70)</th>
<th>Total (N=169)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Female</td>
<td>75</td>
<td>76</td>
<td>60</td>
</tr>
<tr>
<td>Primary language English</td>
<td>49</td>
<td>49</td>
<td>31</td>
</tr>
<tr>
<td>Cognitively impaired</td>
<td>58</td>
<td>59</td>
<td>47</td>
</tr>
<tr>
<td>Experienced cognitive decline</td>
<td>21</td>
<td>21</td>
<td>27*</td>
</tr>
<tr>
<td>Dementia at follow-up</td>
<td>8</td>
<td>8</td>
<td>20***</td>
</tr>
<tr>
<td>Age (years)</td>
<td>75.5</td>
<td>6.9</td>
<td>75.4</td>
</tr>
<tr>
<td>Education (years)</td>
<td>8.2</td>
<td>4.1</td>
<td>6.6*</td>
</tr>
<tr>
<td>Hamilton depression scale scoreb</td>
<td>4.4</td>
<td>5.2</td>
<td>7.3**</td>
</tr>
<tr>
<td>Orientation-memory-concentrationc</td>
<td>5.1</td>
<td>3.7</td>
<td>6.8*</td>
</tr>
<tr>
<td>Functional assessmentd</td>
<td>80.9</td>
<td>22.7</td>
<td>76.0</td>
</tr>
<tr>
<td>Total recalle</td>
<td>34.8</td>
<td>8.2</td>
<td>34.0</td>
</tr>
</tbody>
</table>

aChange in cognition from normal at baseline to impaired or demented at follow-up or from impaired at baseline to demented at follow-up.
bTotal N=119 (71 subjects with no memory complaints and 48 subjects who reported memory complaints at baseline).
cFrom the Blessed Information and Concentration Test, short version (18).
dFrom the Schwab and England Activities of Daily Living Scale (20).
eFrom the Buschke Selective Reminding Test (22).

FIGURE 1. Rate of Dementia Among Community-Dwelling Elderly Individuals at 1-Year Follow-Up, by Baseline Cognitive Category and Baseline Memory Complaints

aDiagnosis of dementia required scores below predetermined cutoff values on neuropsychological tests of memory and on at least two nonmemory tests of cognition, as well as physician-determined functional impairment. Subjects rated as "cognitively impaired" at baseline scored below cutoff values on at least two neuropsychological tests but were not demented.
bSignificant difference between subjects with and without memory complaints at baseline ($\chi^2=11.2$, df=1, $p<0.001$).

As indicated in table 1, the mean educational attainment of normal and impaired subjects differed significantly. Low educational attainment, rather than pathological brain changes, may have accounted for the poor performance on cognitive testing in some subjects (34). To disentangle the effects of cognitive category from those of educational attainment, we repeated our multivariate analyses separately within four subgroups that were defined by median educational attainment (less than 8 years, 8 years or more) and baseline cognitive category

Total recall score at follow-up between subjects with memory complaints and those without memory complaints ($F=0.1$, df=1, 55, $p=0.75$). In contrast, in analyses restricted to the impaired subjects, the adjusted mean total recall score at follow-up of subjects with memory complaints was 4.6 points less than that of subjects without memory complaints ($F=10.0$, df=1, 97, $p=0.002$). We added baseline Hamilton depression scale scores as a continuous covariate to these last analyses. Among normal subjects, memory complaints remained unassociated with a change in total recall ($F=0.2$, df=1, 40, $p=0.69$).

Among cognitively impaired subjects, the adjusted mean total recall score at follow-up of subjects with memory complaints was 3.5 points less than that of subjects without memory complaints, but this difference missed the level of statistical significance ($F=3.1$, df=1, 65, $p=0.08$). However, in these analyses statistical power was reduced because of the exclusion of subjects who lacked a Hamilton depression scale score.

In a logistic regression model adjusted for age, education, and cognitive category, memory complaints were associated with a more than two-fold increase in risk of cognitive decline (odds ratio=2.3, Wald $\chi^2=4.9$, df=1, $p=0.03$). When we added the baseline Hamilton depression scale score as an independent variable to this logistic model, a similar, although statistically nonsignificant, risk estimate associated with memory complaints was obtained (odds ratio=2.0, Wald $\chi^2=2.1$, df=1, $p=0.14$), which indicated a lack of confounding by Hamilton depression scale score. In addition, the Hamilton depression scale score at baseline was unassociated with cognitive decline in this logistic model (odds ratio=1.0, Wald $\chi^2=0.35$, df=1, $p=0.55$). In a separate logistic model adjusted for age, education, memory complaints, and cognitive category that included the interaction between cognitive category and memory complaints, the interaction was associated with an almost four-fold increase in risk of cognitive decline (odds ratio=4.2, Wald $\chi^2=8.0$, df=1, $p=0.01$).
Baseline memory complaints independently contributed to cognitive performance in subjects with baseline cognitive impairment, as well as subjects without memory complaints but only among subjects with baseline cognitive impairment (35). The results of these studies have supported the notion that subjective memory complaints probably have little significance for memory performance. Moreover, however, a longitudinal study that included a substantial number of subjects with borderline cognitive impairment, as well as subjects without memory complaints, found that baseline memory complaints held significant predictive value for dementia at 3 years (35), although the strongest predictor of dementia at follow-up was the initial score on tests of memory.

Our results serve to clarify these apparent discrepancies. We also found an association between depressive symptoms and memory complaints but found little association between memory complaints and memory performance in cross-sectional analyses or between memory complaints and change in performance in subjects with normal cognition. Memory complaints were associated with decline but only among subjects with baseline cognitive impairment. While our diagnostic criteria for dementia included a history of functional impairment, the criteria for cognitive impairment did not. We considered the possibility that in subjects with comparable performance on cognitive testing, subjects with memory complaints...
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Complaints might overstate their functional complaints and would therefore be more likely to receive a dementia diagnosis than subjects without memory complaints. However, a review of the data revealed that, whether or not subjects had memory complaints, all those who met neuropsychological criteria for dementia at follow-up had a history of functional impairment and had been diagnosed as demented.

Before we interpret our findings, some preliminary observations are in order. Cognitive impairment, defined by poor performance on cognitive tests, may reflect low educational attainment or low intelligence without underlying brain pathology or transient, static, or progressive brain diseases. Which of these mechanisms accounts for cognitive impairment can be difficult to determine from a single clinical evaluation, although in the absence of low educational attainment, underlying pathology of some kind can be strongly suspected (34). When serial testing shows significant cognitive decline relative to appropriate comparison subjects, however, underlying brain disease can be inferred, without regard to the subject’s educational attainment. In our study, subjects with baseline cognitive impairment were at particular risk for subsequent decline over 1 year if they also had memory complaints. This finding was most apparent among the better-educated subjects (table 3), in whom the baseline cognitive impairment probably reflected, in most instances, a significant decline from their premorbid cognition. These results indicate that a subject’s cognitive history may be prognostically useful when the results of a cognitive evaluation are also available. The results also suggest that the subjective perception of cognitive symptoms may be influenced, in part, by the rate of cognitive decline. Previous investigators have drawn attention to the large numbers of nondemented individuals with objective evidence of cognitive or memory impairment who deny memory problems (3, 6). Our results suggest that these may be individuals who fail to perceive or report problems because their impairment is stable or deteriorating slowly. If correct, this interpretation has implications for the detection of dementing diseases in clinical practice in the community, insofar as subjective memory complaints may initiate a clinical evaluation, and suggests that there may be relative undetection of slowly progressive cognitive decline. Of course, cognitive evaluations are commonly sought by concerned family members or friends, rather than by the individual personally, but a similar principle might operate here as well. In future studies we plan to determine the extent to which subject and informant-derived reports of memory difficulties are associated with the rate of decline in the subjects’ memory and cognition.

There are some limitations to our study. A large proportion of the subjects who agreed to initial testing did not undergo a follow-up evaluation, primarily because of a change in research goals during the course of the study. While this is an obvious methodological weakness, lack of follow-up was nonsystematic, and subjects seen at 1-year follow-up did not differ significantly from those who were evaluated just once. Brain imaging and laboratory blood test results were unavailable for most subjects, and there may have been errors with respect to the etiology of dementia in some cases. Our questioning and documentation of memory complaints were very simple. Nevertheless, they correspond to the kind of inquiry that might be made during the course of a routine general practice consultation.

How generalizable are our results? Our study group comprised relatively few individuals with high school or tertiary education, and in this respect may not have been representative of many other similarly aged communities. Stratified analyses suggested, however, that our results were not a consequence of this demographic peculiarity; indeed, memory complaints among the better-educated subjects with cognitive impairment were of particular salience. Nevertheless, future longitudinal studies will be important to determine if similar findings are obtained in randomly selected cognitively intact and impaired subjects with higher educational attainment. The criteria by which cognitive impairment and dementia are diagnosed may also influence the outcome in such studies.

In summary, we agree with previous investigators who have shown that memory complaints from an individual with normal cognition predict neither memory performance nor cognitive decline. By contrast, memory complaints from a nondemented individual with cognitive impairment may be more informative and may hint at progressive cognitive decline.

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