Risk of Dementia Among White and African American Relatives of Patients With Alzheimer Disease

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Well-established risk factors for the development of Alzheimer disease (AD) in white populations include age, family history, female sex, and the presence of 1 or 2 copies of the apolipoprotein E (APOE) e4 allele.1,2 Family studies have shown that relatives of white AD patients are at greater risk than nonrelatives for the development of dementia, and that these risks are higher with increasing age, female sex, and the likelihood of carrying 1 or 2 copies of the APOE e4 allele.3-6 The risks associated with AD in other US ethnicities and among populations in other countries have been less thoroughly studied, but there is evidence that the incidence of disease, as well as the risk attributable to specific genetic factors such as APOE genotype, may vary considerably among ethnic groups.2,7-10

Context Evidence exists that the incidence of Alzheimer disease (AD), as well as risk attributable to specific genetic factors such as apolipoprotein E (APOE) genotype, may vary considerably among ethnic groups. Family studies of probands with AD offer an opportunity to evaluate lifetime risk of dementia among relatives of these probands.

Objective To compare lifetime dementia risk estimates among relatives of white and African American probands with probable or definite AD.

Design and Setting Risk analysis using data collected by questionnaire and supplemental records between May 1991 and March 2001 at 17 medical centers contributing to the Multi-Institutional Research in Alzheimer’s Genetic Epidemiology Study.

Participants A total of 17 639 first-degree biological relatives and 2474 spouses of 2339 white AD probands, and 2281 first-degree biological relatives and 257 spouses of 255 African American AD probands.

Main Outcome Measures Cumulative risk of dementia by age 85 years, stratified by ethnicity and sex of relatives and by APOE genotype of probands.

Results Cumulative risk of dementia in first-degree biological relatives of African American AD probands by age 85 years was 43.7% (SE, 3.1%), and the corresponding risk in first-degree biological relatives of white AD probands was 26.9% (SE, 0.8%), yielding a relative risk (RR) of 1.6 (95% confidence interval [CI], 1.4-1.9; P < .001). The risk in spouses of African American AD probands of 18.5% (SE, 8.4%) was also higher than the risk in white spouses of 10.4% (SE, 1.7%) but did not reach statistical significance (RR, 1.8; 95% CI, 0.5-6.0; P = .34), likely due to the smaller sample size of African Americans. The proportional increase in risk of dementia among white first-degree biological relatives compared with white spouses of 2.6 (95% CI, 2.1-3.2) was similar to that of 2.4 (95% CI, 1.3-4.4) in African American first-degree biological relatives compared with African American spouses. Female first-degree biological relatives of probands had a higher risk of developing dementia than did their male counterparts, among whites (31.2% vs 20.4%; RR, 1.5; 95% CI, 1.3-1.7; P < .001) as well as among African Americans, although this was not significant among African Americans (46.7% vs 40.1%; RR, 1.2; 95% CI, 0.9-1.7, P = .30). The patterns of risk among first-degree biological relatives stratified by APOE genotype of the probands were similar in white families and African American families.

Conclusion First-degree relatives of African Americans with AD have a higher cumulative risk of dementia than do those of whites with AD. However, in this study, the additional risk of dementia conferred by being a first-degree relative, by being female, or by the probability of having an APOE e4 allele appeared similar in African American and white families. These data provide estimates of dementia risk that can be used to offer counseling to family members of patients with AD.

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Family studies of probands with AD who have been identified by uniform criteria offer an opportunity to evaluate the lifetime risk of dementia among relatives of these probands. Comparisons of risk in biological relatives and nonbiological relatives (such as spouses) can help distinguish genetic from nongenetic factors within families. The impact of APOE genotype on the risk of dementia among relatives can be assessed indirectly by stratifying the lifetime risk estimates among biological relatives according to the APOE genotype of the proband. We have collected these types of data for 10 years within the Multi-Institutional Research in Alzheimer’s Genetic Epidemiology (MIRAGE) study, and the lifetime risk estimates obtained in white populations have already provided clinically applicable estimates of risk among first-degree relatives in families of white patients with AD.13,14

We have now collected family history data on the largest number of African American families ever studied for AD, to our knowledge. In this study, we report the lifetime risk estimates of dementia for the first-degree biological relatives of probands with AD by ethnicity, and examine the additional risk of dementia conferred on relatives by being female and by the probability of having an APOE ε4 allele. Risk estimates generated by this analysis also provide empirical data to which clinicians can refer when counseling the relatives of their patients with AD who are concerned about their own risk of developing AD.

### METHODS

#### Participants and Data Collection

The details of MIRAGE Study data collection procedures, protocols for obtaining family histories, and reports demonstrating the validity of proxy reporting in participating families have been published elsewhere.5,11,12 In brief, probands or individuals with probable or definite AD by research criteria19 were identified at specialty clinics for dementia by experienced clinician-researchers at 17 centers between May 1991 and March 2001. The structured and validated MIRAGE questionnaires were distributed to family members to elicit health information and dementia status on the entire family. Information on both patients and family members was supplemented by multiple informants, medical records including autopsy reports, death certificates, and nursing home records. Informed consent was obtained from family members who did not have dementia, and a combination of consent or assent, along with informed consent by proxy, was obtained from participants with dementia.

Family history information was available for 2594 probands meeting criteria for definite or probable AD. Age, sex, and dementia status information was incorporated from 19920 first-degree biological relatives of these probands, as well as from 2731 of the probands’ spouses. Data on other risk factors for AD were elicited as described elsewhere.5,13,14 In a subset of 1331 family members 50 years or older who were reported by family informants not to have dementia, cognitive status was confirmed to be normal in 1298 (97.5%) by the modified Telephone Interview of Cognitive Status (mTICS).15,16

Of the first-degree biological relatives, 4681 were parents of the proband (817 affected), 8474 were siblings (715 affected), and 6765 were children (11 affected). There were 1093 families with at least 1 affected first-degree biological relative, indicating that about 42% of the probands had a family history of AD. Of these 1093 families, 784 (71.7%) had 1 affected first-degree biological relative, 216 (19.8%) had 2 affected first-degree biological relatives, and 93 (8.5%) had more than 2 affected first-degree biological relatives.

Ethnicity of participating families was classified by self-report, then reclassified prior to the analysis following the format of the 1990 US Census.17 This analysis was restricted to families in which the proband met criteria for African American or white ethnicity. Age represented the age at which dementia symptoms began in relatives with dementia, or the age at which information was obtained on relatives who did not have dementia. Blood for APOE genotyping was collected on a subset of 1191 (45.9%) of the probands. A standard polymerase chain reaction procedure18 was used for APOE genotyping. Of these samples, 458 (38.5%) were genotyped as APOE ε2/ε2, ε2/ε3, or ε3/ε3; 561 (47.1%), APOE ε2/ε4 or ε3/ε4; and 172 (14.4%), APOE ε4/ε4. The APOE genotype of the proband was grouped into the following 3 categories: ε2/ε2, ε2/ε3, or ε3/ε3; ε2/ε4 or ε3/ε4; and ε4/ε4 genotypes.

### Statistical Analysis

A maximum likelihood procedure similar to a Kaplan-Meier survival analysis was used to estimate the lifetime risks and age at onset distribution for first-degree biological relatives and spouses of the AD probands.5,19 The Kaplan-Meier method takes into account the possibility that those censored at the time of the study may be susceptible and acquire AD after the study end point and that those who died of a competing risk might have acquired AD if they had survived. Our method incorporates these elements into the analysis, but we additionally incorporate affected individuals with unknown ages of onset and nonaffected individuals with unknown censoring ages, thereby avoiding a downward bias in the estimation of mean onset age that would otherwise occur.19 We used maximum likelihood estimation for 5 groups of individuals: (1) affected individuals with known age of onset, (2) unaffected individuals with known censoring age, (3) affected individuals with unknown onset age but with known censoring age, eg, death, (4) affected individuals without known onset age or censoring age, and (5) unaffected individuals without any censoring information. The expectation-maximization algorithm was applied to take into account censored information. In our analysis, 1459 of the 19920 first-degree biological relatives of probands were included in the analysis that would not have been included in the traditional Kaplan-Meier method.
Asymptotically normal distributions of maximum likelihood statistics were used to compute 2 tests by using parameter estimates for risk and their SEs at the maximum common age of 95 years for each ethnic group, and for comparison across groups using risk by age 85 years.

Risk estimates were calculated with stratification by sex, ethnicity, and both sex and ethnicity of the relatives and spouses. Risk estimates among first-degree biological relatives were also stratified according to APOE genotype category of the proband.

All analyses were performed using SAS software version 8.2 (SAS Institute Inc, Cary, NC).

RESULTS

Cumulative risk was estimated based on information gathered from the families of 2339 white and 255 African American probands. The characteristics of the probands, first-degree biological relatives, and spouses are reported in Table 1. Cumulative risk estimates for first-degree biological relatives, stratified by ethnicity, sex, and by the APOE genotype of the proband, and cumulative risk estimates for spouses stratified by ethnicity are shown in Table 2. Curves illustrating the cumulative risks at different ages are shown in Figure 1, Figure 2, and Figure 3. As shown in Figure 1, the cumulative risk (SE) of dementia to age 95 years among first-degree biological relatives of white probands was 43.7% (1.9%) while the risk of dementia to age 95 years among first-degree biological relatives of African American probands was 57.1% (5.6%) (relative risk [RR], 1.3; 95% confidence interval [CI], 1.03-1.6; \( P < .02 \)).

The results that follow refer to cumulative risks of dementia by age 85 years. The cumulative risk (SE) of dementia among first-degree biological relatives of white probands was 26.9% (0.8%) while the risk of dementia among first-degree biological relatives of African American probands was 43.7% (3.1%) (RR, 1.6; 95% CI, 1.4-1.9; \( P < .001 \)). Data from spouses provided cumulative risk estimates of dementia in a population that shared environmental, but not genetic, background with the proband. The cumulative risk of dementia among spouses of white probands was 10.4% (1.7%) while for spouses of African American probands it was 18.5% (8.4%) (RR, 1.8; 95% CI, 0.5-6.0; \( P = .34 \)). The proportional increase of 2.4 (95% CI, 2.1-3.2) in risk between spouses and first-degree biological relatives of African American probands was very similar to the proportional increase of 2.6 (95% CI, 1.3-4.4) in risk between spouses and first-degree biological relatives of white probands. Within ethnic groups, each of these comparisons was significant (\( P < .005 \) for both).

As shown in Table 2 and Figure 2, among the first-degree biological relatives of probands, women had a greater risk of dementia than men, within each ethnic group. African American women had a 1.2-fold higher risk than African American men (RR, 1.2; 95% CI, 0.9-1.7; \( P = .30 \)) while white women had a 1.5-fold higher risk than white men (RR, 1.5; 95% CI, 1.3-1.7; \( P < .001 \)). The absolute increase in risk among women compared with men was of similar magnitude within each ethnic group as illustrated in Figure 4, although it did not reach significance among African Americans.

Among the 980 white probands with APOE genotyping, 466 (47.6%) had 1 \( \varepsilon 4 \) allele and 124 (12.7%) had the \( \varepsilon 4/\varepsilon 4 \) allele. Among the 211 African American probands with APOE genotyping, 95 (45.0%) had 1 \( \varepsilon 4 \) allele and 48 (22.7%) had the \( \varepsilon 4/\varepsilon 4 \) genotype (Table 1). The risk of AD among white and African American probands and its modification with the \( \varepsilon 4 \) allele is described in a separate report.10 As shown in Table 2 and Figure 3, the \( \varepsilon 4 \) status of the pro-

### Table 1. Characteristics of Probands, First-Degree Biological Relatives, and Spouses

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All</th>
<th>White</th>
<th>African American</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probands No.</td>
<td>2594</td>
<td>2339</td>
<td>255</td>
</tr>
<tr>
<td>Age at onset, mean (SD), y</td>
<td>70.0</td>
<td>69.9</td>
<td>71.3 (7.6)</td>
</tr>
<tr>
<td>Education, mean (SD), y</td>
<td>12.1</td>
<td>12.3</td>
<td>10.0 (4.2)</td>
</tr>
<tr>
<td>Women, No. (%)</td>
<td>1601</td>
<td>1416</td>
<td>185 (72.6)</td>
</tr>
<tr>
<td>Blood samples, No. (%)</td>
<td>1191</td>
<td>980</td>
<td>211 (82.7)</td>
</tr>
<tr>
<td>( \varepsilon 2/\varepsilon 2 ) or ( \varepsilon 2/\varepsilon 3 ) or ( \varepsilon 3/\varepsilon 3 )†</td>
<td>458</td>
<td>390</td>
<td>68 (32.2)</td>
</tr>
<tr>
<td>( \varepsilon 2/\varepsilon 4 ) or ( \varepsilon 3/\varepsilon 4 )†</td>
<td>561</td>
<td>466</td>
<td>95 (45.0)</td>
</tr>
<tr>
<td>( \varepsilon 4/\varepsilon 4 )†</td>
<td>172</td>
<td>124</td>
<td>48 (22.7)</td>
</tr>
</tbody>
</table>

#### First-Degree Biological Relatives

<table>
<thead>
<tr>
<th>Affected No.</th>
<th>1543</th>
<th>1323</th>
<th>220</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset, mean (SD), y</td>
<td>74.4</td>
<td>74.5</td>
<td>74.0 (8.3)</td>
</tr>
<tr>
<td>Women, No. (%)</td>
<td>1023</td>
<td>883</td>
<td>140 (63.6)</td>
</tr>
<tr>
<td>Unaffected No.</td>
<td>18</td>
<td>16</td>
<td>2061</td>
</tr>
<tr>
<td>Age, mean (SD)†</td>
<td>58.7</td>
<td>58.9</td>
<td>57.3 (17.8)</td>
</tr>
<tr>
<td>Women, No. (%)</td>
<td>9058</td>
<td>8099</td>
<td>1049 (50.9)</td>
</tr>
</tbody>
</table>

#### Spouses

<table>
<thead>
<tr>
<th>Affected No.</th>
<th>76</th>
<th>68</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset, mean (SD), y</td>
<td>75.8</td>
<td>75.2</td>
<td>82.0 (4.5)</td>
</tr>
<tr>
<td>Women, No. (%)</td>
<td>18</td>
<td>15</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>Unaffected No.</td>
<td>2656</td>
<td>2406</td>
<td>249</td>
</tr>
<tr>
<td>Age, mean (SD)†</td>
<td>73.4</td>
<td>72.5</td>
<td>78.6 (9.8)</td>
</tr>
<tr>
<td>Women, No. (%)</td>
<td>1057</td>
<td>983</td>
<td>74 (29.7)</td>
</tr>
</tbody>
</table>

†Percentages expressed as percentage of the group with a blood sample.
†Age at data collection or death.
for the educational level of the proband, the risk estimates in relatives were stratified by educational level among both whites and African Americans (data not shown). The risk estimates for relatives of African American probands were higher within each strata of proband education than the same estimates in whites. Therefore, educational levels of the probands do not confound the risk differences observed between ethnicities.

**COMMENT**

In the clinical setting, family members of patients with AD realize that AD has a heritable component, and they often ask the clinician for some measure of their own risk. This report provides clinically relevant estimates of dementia risk in a large clinic-based population of white and African American families. These data confirm and enhance the precision of the cumulative risk curves that we have already published for white families. Our large sample of African American families allows us to present, for the first time, precise age-specific risks of dementia among first-degree biological relatives of African American patients with AD. By examining the risk curves for relatives in Figure 1, clinicians can now ascertain empirical estimates of risk that may be useful for counseling white and African American family members of AD patients.

Our data indicate that relatives of African American patients are 1.6 times more likely than relatives of white patients to become demented by age 85 years. This finding could potentially reflect a higher degree of familial aggregation in African American families, a

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### Table 1. Estimated Cumulative Risk of Dementia Among First-Degree Biological Relatives and Spouses of Alzheimer Disease Probands*

<table>
<thead>
<tr>
<th>Comparison Groups</th>
<th>No. of Probands</th>
<th>Age at Onset, Mean (SE), y</th>
<th>Oldest Onset Age Among Affected Biological Relatives, y</th>
<th>Comparison Risk at 85 Years (SE)</th>
<th>Comparison RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-degree blood relatives</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African Americans</td>
<td>255</td>
<td>220</td>
<td>2061</td>
<td>79.9 (1.2)</td>
<td>95</td>
</tr>
<tr>
<td>Whites</td>
<td>2339</td>
<td>1323</td>
<td>16316</td>
<td>82.3 (0.6)</td>
<td>96</td>
</tr>
<tr>
<td>Spouses</td>
<td>247</td>
<td>8</td>
<td>249</td>
<td>85.6 (1.6)</td>
<td>89</td>
</tr>
<tr>
<td>Whites</td>
<td>2221</td>
<td>68</td>
<td>2406</td>
<td>82.0 (1.3)</td>
<td>90</td>
</tr>
<tr>
<td>Spouses</td>
<td>2221</td>
<td>68</td>
<td>2406</td>
<td>82.3 (0.6)</td>
<td>96</td>
</tr>
<tr>
<td>African Americans</td>
<td>247</td>
<td>8</td>
<td>249</td>
<td>85.6 (1.6)</td>
<td>89</td>
</tr>
<tr>
<td>Spouses</td>
<td>247</td>
<td>8</td>
<td>249</td>
<td>85.6 (1.6)</td>
<td>89</td>
</tr>
<tr>
<td>First-degree blood relatives</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whites</td>
<td>2312</td>
<td>883</td>
<td>8009</td>
<td>82.2 (0.6)</td>
<td>96</td>
</tr>
<tr>
<td>Men</td>
<td>2308</td>
<td>440</td>
<td>8307</td>
<td>81.9 (1.3)</td>
<td>96</td>
</tr>
<tr>
<td>African Americans</td>
<td>252</td>
<td>140</td>
<td>1049</td>
<td>79.7 (1.2)</td>
<td>95</td>
</tr>
<tr>
<td>Men</td>
<td>248</td>
<td>80</td>
<td>1012</td>
<td>78.5 (1.3)</td>
<td>89</td>
</tr>
</tbody>
</table>

**Comparison Among White First-Degree Blood Relatives**

<table>
<thead>
<tr>
<th>APOE genotype of the proband</th>
<th>No of Relatives</th>
<th>Age at Onset, Mean (SE), y</th>
<th>Oldest Onset Age Among Affected Biological Relatives, y</th>
<th>Comparison Risk at 85 Years (SE)</th>
<th>Comparison RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>e2/e4 or e3/e4</td>
<td>466</td>
<td>322</td>
<td>3020</td>
<td>79.9 (1.0)</td>
<td>95</td>
</tr>
<tr>
<td>e4/e4</td>
<td>124</td>
<td>90</td>
<td>851</td>
<td>78.6 (1.2)</td>
<td>90</td>
</tr>
<tr>
<td>e2/e2 or e2/e3 or e3/e3</td>
<td>390</td>
<td>190</td>
<td>2691</td>
<td>84.2 (1.3)</td>
<td>96</td>
</tr>
</tbody>
</table>

**Comparison Among African First-Degree Blood Relatives**

<table>
<thead>
<tr>
<th>APOE genotype of the proband</th>
<th>No of Relatives</th>
<th>Age at Onset, Mean (SE), y</th>
<th>Oldest Onset Age Among Affected Biological Relatives, y</th>
<th>Comparison Risk at 85 Years (SE)</th>
<th>Comparison RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>e2/e4 or e3/e4</td>
<td>95</td>
<td>101</td>
<td>762</td>
<td>81.0 (1.9)</td>
<td>95</td>
</tr>
<tr>
<td>e4/e4</td>
<td>48</td>
<td>42</td>
<td>362</td>
<td>77.1 (1.1)</td>
<td>85</td>
</tr>
<tr>
<td>e2/e2 or e2/e3 or e3/e3</td>
<td>68</td>
<td>57</td>
<td>616</td>
<td>78.9 (1.8)</td>
<td>90</td>
</tr>
</tbody>
</table>

*RR indicates relative risk; CI confidence interval; and APOE, apolipoprotein E.
higher baseline risk of dementia, or both. These possibilities can be distin-
guished by examining the risk of de-
mentia among spouses of our AD pa-
tients who are matched by age and share many environmental determinants. We
find that spouses of African American patients with AD are 1.8 times more
likely to develop dementia than spouses
of white patients, and that the propor-
tionate additional risk conferred by being
a first-degree relative is quite similar in
each ethnic group (2.6 in whites vs 2.4
in African Americans). Thus we con-
clude that risk attributable to familial ag-
gregation is very similar in African
American families and white families.

As shown in Table 2 and Figure 2,
female relatives are at higher risk than
male relatives. Figure 4 suggests that
while the risk associated with African
American ethnicity is much larger than
that associated with sex of the rela-
tive, the degree to which sex influ-
ences risk within each ethnic group is
similar.

In the subset of AD patients for
whom we assessed APOE genotype, we
were also able to calculate risks in re-
latives stratified by the genotype of the
patient. Although the genotypes of the
relatives themselves were not avail-
able, this stratification serves as an es-
timate of the probability of finding an
ε4 allele in the relatives of each strata.5
Figure 3 and Figure 5 once again sug-
gest that ethnicity is a more powerful
risk factor for dementia in relatives than
the presence of an ε4 allele in the pro-
band. And, although the curves im-
plied in Figure 5 are not completely par-
allel, with relatively wide SEs around
the point estimates in the African
American relatives, they too suggest that
the increase among relatives that can
be attributed to the probability of hav-
ing an ε4 allele is quite similar in both
ethnic groups.

The only other study to estimate fa-
milial risk in African American fami-
lies solicited family history informa-
tion from incident cases of AD and
controls in a community-based study
of white, African American, and Carib-
bean Hispanics in northern Manhat-
tan.20,21 Devi et al12 studied 57 white
patients with AD with 219 relatives and
112 African American patients with AD
with 362 relatives but did not report cu-
mulative risk estimates by ethnicity.
They used Cox proportional hazard
analysis to adjust for proband's sex, edu-
cational level, and the sex of the rela-
tives, to calculate adjusted rate ratios.
They found relatives of white patients
to have a rate ratio of 2.0 (95% CI, 1.2-
3.3) compared with the relatives of con-
trols, and the relatives of African Ameri-
can patients to have a rate ratio of 1.4
(95% CI, 0.7-2.7) compared with the
relatives of controls. No comparisons
were drawn between the risks to Afri-
can American relatives and the risks to
white relatives of AD patients. The mag-
nitude of the increase in risk between

Figure 1. Cumulative Risk of Dementia in First-Degree Biological Relatives and in Spouses of
Probands, Stratified by Ethnicity of Probands

Figure 2. Cumulative Risk of Dementia in First-Degree Biological Relatives of Alzheimer
Disease Probands, Stratified by Relatives’ Sex and Ethnicity

Error bars indicate SE.
the relatives of their patients compared with the relatives of their controls is similar to the magnitude of increased risk among both white and African American relatives in our study in comparison to spouses.

In a population of 101 white patients and 195 African American patients, Devi et al also examined the additional risk conferred by the presence of an e4 allele in the proband. Direct comparisons with our results are not straightforward because they did not compare risk across ethnic groups, and their data were stratified by the presence of at least 1 e4 allele while ours were stratified into 3 groups (no, 1, or 2 e4 alleles). Among relatives of patients with AD, Devi et al found that the presence of at least 1 e4 allele doubled the adjusted risk among whites and tripled the adjusted risk among African Americans, which appears consistent with our findings.

Our findings are based on cross-sectional data from clinic-based recruit-
Dementia Risk Among Relatives of Patients with AD

The association between APOE genotype and risk of AD is well established in white populations, and the association in African Americans and in whites is higher in African Americans than in whites. However, within each ethnic group, the additional risk conferred by being a first-degree biological relative, by being female, or by the probability of having an ε4 allele is of very similar magnitude. Our data provide estimates of dementia risk that can be used to provide counseling to family members of patients with AD.

In conclusion, our findings in this report support the growing body of data that risk of dementia and AD is higher in African Americans than in whites. However, within each ethnic group, the additional risk conferred by being a first-degree biological relative, by being female, or by the probability of having an ε4 allele is of very similar magnitude. Our data provide estimates of dementia risk that can be used to provide counseling to family members of patients with AD.

Implications

A number of epidemiological studies have examined the risk of dementia or of AD in white and African American people, and recent studies have consistently supported a higher age-specific prevalence of dementia, cumulative risk of AD, and incidence rates of AD among African Americans compared with non-Hispanic whites. Most relevant to our findings, Tang et al reported that the cumulative risk of AD among African Americans by age 90 years is 4 times that of whites.

The association between APOE genotype and risk of AD is well established in white populations, and the association in African Americans is of great interest. A number of studies have suggested a weaker association between ε4 and AD in African Americans than in whites as well as a weaker association among elderly Nigerians and Kenyans. The data on risk in family members presented in this article do not address this question, but our analysis of APOE information from a large group of MIRAGE probands, siblings, and unrelated controls indicates that ε4 is an important risk factor for AD in African Americans, particularly among those younger than 70 years. Taken together, our data suggest that genetic factors other than APOE play an important role in the heritable component of AD in both white and African American families.

Figures 1 and 2 provide clinicians with information that can be used to advise family members of patients with AD who ask about their own average risk of developing dementia. Figure 1 provides a contrast between the average risk of a first-degree biological relative and that of the general population, as estimated through the spouses of probands, although this should be interpreted with caution because spouses are not truly representative of the population at large and because the number of affected African American spouses is so low. Figure 2 provides the most refined category of risk estimate, stratified by ethnicity and sex. Because APOE genotyping is not currently advocated to help estimate risk, Figure 3 is of scientific interest but should not be used for clinical counseling.

REFERENCE


8. Gao S, Hendrie HC, Hall KS, Hu L. The relationships between age, sex, and the incidence of dementia...
Flowers changed the face of the planet. Without them, the world we know—even man himself—would never have existed. Francis Thompson, the English poet, once wrote that one could not pluck a flower without troubling a star. Intuitively he had sensed like a naturalist the enormous interlinked complexity of life.

Today we know that the appearance of the flowers contained also the equally mystifying emergence of man.

—Loren Eiseley (1907-1977)