Earlier Onset of Alzheimer Disease Symptoms in Latino Individuals Compared With Anglo Individuals

Christopher M. Clark, MD; Charles DeCarli, MD; Dan Mungas, PhD; Helena I. Chui, MD; Roger Higdon, PhD; Jessica Nuñez; Héritique Fernandez, MD; Mirna Negron, BSW; Jennifer Manly, PhD; Steven Ferris, PhD; Angelica Perez, PhD; Migdalia Torres, MSW; Douglas Ewbank, PhD; Giulia Glosser, PhD; Gerald van Belle, PhD

Background: Latino individuals are the largest minority group and the fastest growing population group in the United States, yet there are few studies comparing the clinical features of Alzheimer disease (AD) in this population with those found in Anglo (white non-Latino) patients.

Objective: To compare the age at AD symptom onset in Latino and Anglo individuals.

Design: Cross-sectional assessment using standardized methods to collect and compare age at AD symptom onset, demographic variables, and medical variables.

Setting: Five National Institute on Aging–sponsored Alzheimer’s Disease Centers with experience evaluating Spanish-speaking individuals.

Patients: We evaluated 119 Latino and 55 Anglo patients who had a diagnosis of AD.

Main Outcome Measure: Age at symptom onset.

Results: After adjusting for center, sex, and years of education, Latino patients had a mean age at symptom onset 6.8 years earlier (95% confidence interval, 3.5-10.3 years earlier) than Anglo patients.

Conclusions: An earlier age at symptom onset suggests that US mainland Latino individuals may experience an increased burden of AD compared with Anglo individuals. The basis for the younger age at symptom onset remains obscure.

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The evaluation of dementia in Latino patients presents a challenge to both community health care professionals and physicians at dementia specialty clinics. Although it is not surprising that language barriers can lead to diagnostic errors and misinterpretation of the symptoms of dementia, it is also possible that clinical criteria developed in Anglo populations to detect the earliest changes of cognitive impairment may not be as reliable or informative when used in other population groups. In addition, English-language psychometric age- and education-adjusted norms used to assess memory, language, and constructional praxis may not have the same performance characteristics when applied to Spanish-language subjects. This is especially important with respect to the assessment of older Latino individuals. Spanish is the principal language of 94% of Cuban Americans, 86% of Mexican Americans, 76% of Hispanic Americans, and 91% of Puerto Ricans living in the US mainland. The psychometric assessment is further compounded by the fact that elderly Latino people make up the highest proportion of individuals in any US population group who have not attained a high school education. Finally, a low caregiver education level may be associated with a failure to recognize the initial signs and symptoms of dementia.

The Alzheimer’s Disease Centers (ADC) program was established by the National Institute on Aging (Bethesda, Md) to promote clinical and basic investigations in AD. Minority-focused clinics were incorporated into the program in an effort to extend the investigation of neurodegenerative dementias to all population groups in the United States. This study represents the first attempt to compare a major clinical feature of AD (the age at symptom onset) between the Latino and Anglo subjects evaluated through the ADC program.

The first phase of the study involved a nonstandardized retrospective comparison of the age at AD symptom onset registered in the database for all Latino and Anglo patients evaluated at the 5 participating ADCs. The second phase involved an expanded cross-sectional prospective comparison of Latino and Anglo patients with a clinical diagnosis of probable or possible AD. Using standardized assessment tools, the age at AD symptom onset and demographic and medical information were obtained for Latino and Anglo individuals with a clinical diagnosis of probable or possible AD who were evaluated at 3 East Coast (University of Pennsylvania, Columbia University, and New York University) and 2 West Coast (University of Southern California and University of California, Davis) ADC clinics.

Latino and Anglo patients who met standard diagnostic criteria for probable or possible AD and a knowledgeable informant willing to participate were eligible for inclusion. To reduce potential bias based on factors that affect the length of time patients maintained contact with the clinic, those whose first ADC evaluation occurred prior to January 1, 1998, were excluded from the study. To reduce the expected difference in formal education between the 2 cohorts, Anglo individuals with more than 12 years of schooling were excluded. The knowledgeable informant, usually the patient’s spouse or adult child, participated in the standardized structured interview used to determine the age at AD symptom onset. In addition, the informant confirmed or provided demographic information for each participating patient, including birthplace, migration history, and years of formal education, and provided the information needed to complete the Blessed Dementia Scale, the Neuropsychiatric Inventory (short form), the Dementia Severity Rating Scale, and for Latino patients, the Acculturation Severity Rating Scale (short form). The severity of the patient’s cognitive impairment was determined using the MMSE, and symptoms of depression were assessed using the Geriatric Depression Scale (short form).

An investigator meeting was held prior to the start of the study to ensure that the assessment protocol was administered in a standard manner. Using a Web-based interface, data collected at each site were entered into the study database developed and maintained by the National Alzheimer’s Coordinating Center at the University of Washington.

**STATISTICAL ANALYSIS**

Age at AD symptom onset was the primary response variable and was calculated as the patient’s age when the first symptom was noted, as determined by the knowledgeable informant’s responses during the age-at-onset structured interview. Models were fitted using multiple linear regression, including terms for race, sex, education, and center. Other factors and interactions were examined by adding them to this model one at a time.

One concern was that differences in observed mean age at onset could be due to differences in the age distributions of Latino and Anglo individuals in the catchment areas for the 5 centers. To test this hypothesis, we calculated estimated mean ages at onset for the Latino and Anglo populations by applying published AD incidence rates to 2000 US Census data for the metropolitan areas surrounding each of the 5 participating ADCs. These estimates rely only on the relative incidence rates at each age and would not be affected by changes in the level of incidence.

The retrospective database analysis revealed that the mean age at symptom onset for 366 Latino patients with a clinical diagnosis of AD was 68.8 years compared with 73.5 years for 2823 Anglo patients. The reason for the 4.7-year difference did not vary between the East Coast (predominantly Caribbean) and West Coast (predominantly Mexican) sites.

In the second phase of the study, 119 Latino and 55 Anglo patients were prospectively evaluated using standardized assessment tools. There were no differences between the Latino and Anglo cohorts in sex distribution, the proportion with a diagnosis of probable vs possible AD, or the severity of cognitive impairment as measured by MMSE score at the time of enrollment (Table 1). Despite the exclusion of Anglo individuals with more than 12 years of schooling, the mean level of education still differed by 4 years.

After adjusting for center, sex, and years of education, the mean age at onset for the first dementia symptom was 6.8 years (95% confidence interval [CI], 3.5-10.3 years) earlier in Latino compared with Anglo patients (Table 2). This difference in the mean age at onset did not vary by center ($P = .27$). In addition, the difference in age at onset by ethnic status was not significant when
The comparisons were restricted to subjects from either the East or West Coast centers.

Latino patients had less formal education than Anglo patients (7.3 years vs 11.3 years). The level of education had a modest effect on the age at symptom onset; the difference between Latino and Anglo patients became less evident as the years of education increased \((P = .03)\). For example, the estimated difference was 10.0 years with 7 years of education but only 6.5 years with 11 years of education. For Anglo patients, the age at symptom onset decreased with increasing years of education \((P = .004)\), whereas for Latino patients alone, the relationship between age at onset and years of education did not reach statistical significance. The fact that participants with the lowest education level tended to be Latino introduced confounding between education and ethnicity. Nevertheless, even when the analysis was restricted to Anglo and Latino patients with more than 7 years of education, the difference in age at symptom onset was 7.2 years (95% CI, 3.7-10.7 years).

There was a high correlation between the age at symptom onset and the age when the patient participated in this study \((r = .87)\), indicating that the results of the analysis would not change if age at enrollment into the study were substituted for age at symptom onset. The mean difference between Anglo and Latino patients did not change significantly after controlling for whether or not memory impairment was reported as the first symptom, the patient’s Geriatric Depression Scale score at the time of enrollment in the study, or whether the patient was already an ADC subject at the time of evaluation (Table 3).

The 2 cohorts differed with respect to the prevalence of comorbid conditions. Latino patients were more likely to have hypertension (39% vs 18%) and diabetes (22% vs 13%) than Anglo patients. There was little difference between Latino and Anglo patients in MMSE scores or the subjective rating of the quality of the knowledgeable informant’s response to the standardized symptom onset assessment instrument. There was a modest association between the reported age at symptom onset and the knowledgeable informant’s relationship to the patient (spouse vs adult child) and the informant’s years of formal education. For both Latino and Anglo patients, there was a tendency for the reported age at onset to be slightly higher when the informant was an adult child \((P = .03)\). There was a significant difference between the 2 cohorts in the knowledgeable informant’s level of education (12.2 years for Latino individuals vs 14.3 years for Anglo individuals; \(P = .005\); 95% CI, 0.9-3.4). Although the age reported for the onset of symptoms significantly increased with an increase in the years of education of the informant \((P = .005)\), this relationship did not modify the effect of ethnicity. There was no evidence of a relationship between the degree of acculturation in the Latino cohort and age at onset (data not shown). There was no difference in the age at symptom onset between the predominantly Puerto Rican East Coast Latino individuals and the predominantly Mexican Latino individuals evaluated at the 2 California ADCs.

When the patients enrolled in this study were compared with all patients with a clinical diagnosis of probable or possible AD who were evaluated at the participating ADCs during the previous 3 years, the only difference was a lower proportion of men (18% vs 34%) in the age-at-onset study, particularly among the Anglo cohort (33.8% in the ADCs vs 14.2% in this study). Both the age-at-onset study cohort and the much larger total ADC cohort were similar in terms of age calculated as of September 1, 2001 (data not shown).

On average, Latino individuals older than 50 years living in the communities from which the study cohorts were drawn are 3.4 years younger (mean age, 62.4 years) than their Anglo neighbors (mean age, 65.8 years). Estimating the difference in age at onset using published AD incidence rates\(^{36}\) with the assumption that the incidence rates are the same for white and Latino individuals yields a difference of about 1.8 years (26% of the 6.8-year difference between the 2 cohorts in the age at AD symptom onset found in this study).

### Table 1. Cohort Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Latino</th>
<th>Anglo</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>119</td>
<td>55</td>
</tr>
<tr>
<td>Female, No.</td>
<td>75</td>
<td>78</td>
</tr>
<tr>
<td>Education, y</td>
<td>7.3</td>
<td>11.3</td>
</tr>
<tr>
<td>Proportion with probable AD, %</td>
<td>84</td>
<td>89</td>
</tr>
<tr>
<td>MMSE score at age-at-onset assessment</td>
<td>12.1</td>
<td>11.9</td>
</tr>
</tbody>
</table>

Abbreviations: AD, Alzheimer disease; MMSE, Mini-Mental State Examination.

### Table 2. Age at Onset

<table>
<thead>
<tr>
<th></th>
<th>Latino</th>
<th>Anglo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Age at Symptom Onset, y</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>67.6</td>
<td>73.1</td>
</tr>
<tr>
<td>Patients with education (\geq 8) y</td>
<td>65.2</td>
<td>72.7</td>
</tr>
<tr>
<td><strong>Mean Difference (95% CI), y</strong></td>
<td>6.8 (3.5-10.3)</td>
<td>7.2 (3.7-10.7)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

*Unadjusted for center, sex, and years of education.
†Adjusted for center, sex, and years of education.

### Table 3. Potential Confounders

<table>
<thead>
<tr>
<th></th>
<th>Latino</th>
<th>Anglo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory loss as first complaint, No. of patients</td>
<td>56</td>
<td>62</td>
</tr>
<tr>
<td>Geriatric Depression Scale score</td>
<td>4.8</td>
<td>3.5</td>
</tr>
<tr>
<td>No. of comorbid medical conditions*</td>
<td>0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>First contact in the ADC, No. of patients</td>
<td>84</td>
<td>93</td>
</tr>
</tbody>
</table>

Abbreviation: ADC, Alzheimer’s Disease Center.

*Includes hypertension, cardiac disease, diabetes, and cerebrovascular disease.
ADC dementia specialty clinics had a mean age at symptom onset that was 6.8 years earlier than Anglo individuals evaluated at the same clinics. The explanation for the earlier age at symptom onset remains uncertain. The difference between the 2 cohorts remained significant after adjustment for education and demographically related age differences in the portion of each cohort at risk for AD. This earlier mean age at symptom onset suggests that US mainland Latino individuals may experience an increased burden of AD compared with Anglo people. It is not known if there are comparable differences between these 2 groups in the rate of symptom progression or total duration of AD.

There was no difference in the age at symptom onset between the East Coast Latino patients (primarily of Caribbean origin) and the predominantly Mexican American Latino patients evaluated by the 2 California ADCs. In addition, although an analysis of the baseline data from a Sacramento, Calif, epidemiological cohort study found a higher risk for dementia in Latino individuals with type 2 diabetes and stroke, in our study there was no indication that the younger age at onset in Latino patients was associated with potential confounders such as depression, the increased prevalence of comorbid medical conditions, differences in years of education, or the degree to which Latino patients or informants retained aspects of their culture.

There are several cautions in applying the results of this study to the general population. Both the Latino and Anglo cohorts represented samples of convenience, meaning that they were drawn from individuals attending a dementia specialty clinic and therefore cannot be considered representative of the overall US mainland population. Although there are no published studies on the relationship between age at onset and years of education in Anglo individuals with 12 years of education or less, the association of an older age at onset with fewer years of education in our Anglo subjects suggests that they may not be representative of all low-education Anglo patients with AD in the US mainland. In addition, the quality of education may have differed between the Latino and Anglo cohorts and may have been a more relevant marker than the number of years spent in school.

Not addressed in the study design was the possibility that a portion of the observed difference in age at onset could be due to US mainland demographic differences in the age distribution between the Latino and Anglo cohorts. However, if the age-specific incidence rates for Latino individuals are proportional to those for Anglo individuals, demographic difference would account for only 26% of the difference in age at onset observed between the 2 groups.

Measurement error and unappreciated bias in the symptom onset instrument may also confound the results, particularly if there is an unrecognized bias toward a particular group. In addition, socioeconomic and family stress associated with migration and integration into the Anglo-dominant mainland culture may bring out symptoms of depression and anxiety during the prodromal phase of AD, and this may not have been adequately captured. Finally, unmeasured confounders are always a problem in observational studies.

Despite these cautions, the findings in this study indicate that Latino individuals, the largest and fastest growing minority group in the mainland United States, appear to have an earlier age of AD symptom onset compared with Anglo individuals with a similar educational level. The factors responsible for this remain to be identified, but the observation has a potential impact on both the burden of dementia care carried by this population group and the dementia-related diagnostic and educational efforts directed toward the Latino population. From the individual patient and family standpoint as well as a public health perspective, it is important to identify modifiable factors that contribute to the symptomatic expression of AD in this significant minority group.

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Author Affiliations: Department of Neurology (Drs Clark and Glosser), Alzheimer’s Disease Center (Drs Clark, Fernandez, Ewbank, and Glosser and Mss Nuñez and Negrón), and the Population Studies Center (Dr Ewbank), University of Pennsylvania, Philadelphia; Department of Neurology, Sergievsky Center, and Alzheimer’s Disease Research Center (Dr Manly), Columbia University, New York, NY; Alzheimer’s Disease Center (Drs Ferris and Perez and Ms Torres), New York University, New York; Department of Neurology and Alzheimer’s Disease Research Center (Dr Chui), University of Southern California, Los Angeles; Department of Neurology and Alzheimer’s Disease Center (Drs DeCarli and Mungas), University of California, Davis; and the National Alzheimer’s Coordinating Center (Drs Higdon and van Belle), University of Washington, Seattle.

Correspondence: Christopher M. Clark, MD, 3615 Chestnut St, Philadelphia, PA 19104 (clarkc@mail.med.upenn.edu).

Author Contributions: Study concept and design: Clark, Mungas, Chui, Fernandez, Manly, Perez, Ewbank, Glosser, and van Belle. Acquisition of data: DeCarli, Mungas, Chui, Nuñez, Fernandez, Negrón, Manly, Ferris, Perez, Torres, and van Belle. Analysis and interpretation of data: Clark, DeCarli, Chui, Higdon, Nuñez, Fernandez, Manly, Perez, Ewbank, and van Belle. Drafting of the manuscript: Clark, Nuñez, Fernandez, Torres, and Glosser. Critical revision of the manuscript for important intellectual content: Clark, DeCarli, Mungas, Chui, Higdon, Nuñez, Fernandez, Negrón, Manly, Ferris, Perez, Ewbank, Glosser, and van Belle. Statistical analysis: Clark, Higdon, Ewbank, and van Belle. Obtained funding: Clark, Mungas, and Manly. Administrative, technical, and material support: Clark, DeCarli, Mungas, Chui, Fernandez, Manly, Ferris, and Torres. Study supervision: Clark, Chui, Nuñez, Fernandez, Manly, and Glosser.

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