## Bilingualism delays age at onset of dementia, independent of education and immigration status

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#### ABSTRACT

**Objectives:** The purpose of the study was to determine the association between bilingualism and age at onset of dementia and its subtypes, taking into account potential confounding factors.

**Methods:** Case records of 648 patients with dementia (391 of them bilingual) diagnosed in a specialist clinic were reviewed. The age at onset of first symptoms was compared between monolingual and bilingual groups. The influence of number of languages spoken, education, occupation, and other potentially interacting variables was examined.

**Results:** Overall, bilingual patients developed dementia 4.5 years later than the monolingual ones. A significant difference in age at onset was found across Alzheimer disease dementia as well as frontotemporal dementia and vascular dementia, and was also observed in illiterate patients. There was no additional benefit to speaking more than 2 languages. The bilingual effect on age at dementia onset was shown independently of other potential confounding factors such as education, sex, occupation, and urban vs rural dwelling of subjects.

**Conclusions:** This is the largest study so far documenting a delayed onset of dementia in bilingual patients and the first one to show it separately in different dementia subtypes. It is the first study reporting a bilingual advantage in those who are illiterate, suggesting that education is not a sufficient explanation for the observed difference. The findings are interpreted in the context of the bilingual advantages in attention and executive functions. *Neurology*® 2013;81:1938-1944

#### GLOSSARY

ACE-R = Addenbrooke's Cognitive Examination-revised; AD = Alzheimer disease; CDR = Clinical Dementia Rating; DLB = dementia with Lewy bodies; FTD = frontotemporal dementia; GLM = general linear model; VaD = vascular dementia.

Recent studies suggest that bilingualism may delay the age at onset of dementia due to Alzheimer disease (AD) dementia by up to 5 years.<sup>1-4</sup> The potential mechanism is suggested by emerging literature demonstrating that lifelong factors enhancing premorbid cognitive ability delay the expression of dementia.<sup>5</sup> A bilingual cognitive advantage in executive functioning has also been demonstrated.<sup>6-9</sup> However, many crucial questions remain unanswered. The protective effect of bilingualism has only been established in AD dementia and it is unclear whether it extends to other dementia subtypes. The bilingual effect has so far mainly been observed in immigrant populations, making it difficult to disentangle the phenomenon of bilingualism from biological as well as environmental differences.<sup>1-3</sup> Furthermore, the additional benefit of knowing more than 2 languages is unresolved.<sup>2</sup>

These questions can be addressed by studying populations in which bilingualism forms part of everyday life of the autochthonous population. Such a situation exists in India, a country characterized by an exceptional linguistic diversity.<sup>10</sup> Several aspects of Indian bilingualism are important in the context of this study. First, bilingualism does not tend to be associated with immigration. Languages are usually acquired simultaneously and used in parallel and language switching is very common.<sup>11,12</sup> Furthermore, bilingualism in India is contact-based and motivated by socialization processes and is therefore found even among those who are

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illiterate.<sup>13,14</sup> Based on this unique social and linguistic setting, we aimed to study the association between bilingualism and age at dementia and its subtypes, taking into account potential confounding factors.

METHODS Patients. Case records of consecutive patients with dementia diagnosed in a specialist Memory Clinic of a university hospital in Hyderabad between June 2006 and October 2012 were reviewed. All patients were participants of a longitudinal ongoing dementia registry project initiated with an aim to evaluate dementia patients with clinical, imaging, and follow-up studies. The patient profile is representative of the pattern seen at a tertiary, referral neurology service in an Indian city. All subjects were evaluated by an experienced behavioral neurologist (S.A.) using a diagnostic protocol adapted from the Cambridge Memory Clinic model.<sup>15</sup> The assessments were performed by trained psychologists using a structured procedure. The Mini-Mental State Examination, Addenbrooke's Cognitive Examination-revised (ACE-R), adapted for Telugu-, Dakkhini-, and the Hindi-speaking populations in Hyderabad, and the Clinical Dementia Rating (CDR) scale were used to assess patients.<sup>16</sup> Diagnosis of dementia and its subtypes was made based on standard criteria.16

For the present study, case records of patients were reviewed by a research fellow who was not involved with data collection (A.K.S.) for the following details: age of patient, sex, age at onset of dementia, educational status, occupation, rural vs urban dwelling, family history of dementia, history of stroke, and vascular risk factors. All information was obtained from a reliable family member. Age at onset of dementia was defined as the age at which the first clinical symptom suggestive of dementia was observed. Educational status was derived from years of formal education received. Illiterate individuals were defined as those who had no formal education and were unable to read and write in any language. In keeping with the skill levels defined to suit Indian conditions, we used the National Classification of Occupations–2004 to classify subjects into different occupational statuses.<sup>17</sup>

During the study period, 715 patients were diagnosed with dementia due to one of the following causes: AD dementia, frontotemporal dementia (FTD), vascular dementia (VaD), dementia with Lewy bodies (DLB), and mixed dementia. Sufficient demographic or clinical data were missing for 67 patients, either because the family member did not provide the necessary information or patients did not complete the evaluation. The remaining 648 patients were included in the study.

Standard protocol approvals, registrations, and patient consents. The institutional ethics committee of Nizam's Institute of Medical Sciences approved the study.

Language status. In Hyderabad, the majority of the population can be considered as bilingual and many speak 3 or even more languages. Telugu is spoken by the majority group who are primarily Hindus, whereas the language of a minority group of Muslims is Dakkhini. English is gradually acquiring more functional roles in education, administration, and media. In addition, Hindi is spoken as the official national language and is taught at school level. Thus, most people in Hyderabad are exposed to Telugu and Dakkhini in informal contexts and Hindi and English in formal contexts. The patterns of language use in Hyderabad have been systematically studied and are well documented.<sup>11</sup>

As part of the standard protocol, language history was obtained by interviewing a reliable family member. The number of languages spoken fluently by the patient before onset of dementia and the ability of the patient to communicate in these languages were noted from the interview. Bilinguals in this study were defined based on the definition by Mohanty.<sup>18</sup> On synthesizing the several ways in which bilingualism has been articulated and investigated in India, Mohanty defined bilingual persons as those with an ability to meet the communicative demands of the self, and the society in their normal functioning in 2 or more languages in their interaction with the other speakers of any or all of these languages. The native language of each subject was noted. The total number of languages known by each patient was also recorded as 1, 2, 3, or 4 or more.

Statistical analysis. Monolingual and bilingual subject groups were compared across clinical and demographic factors including age of patients, age at onset of dementia, dementia subtypes, education, rural vs urban dwelling, occupation, dementia severity, duration of illness, family history of dementia, vascular risk factors, and stroke. Comparisons between groups of patients were done using an independent samples t test/one-way analysis of variance followed by post hoc tests using Bonferroni adjustments for continuous variables and Fisher exact/ $\chi^2$  test for categorical variables as appropriate. A univariate general linear model (GLM) was used to assess the effect of bilingualism and education on age at onset of dementia after adjusting for various demographic and clinical variables. Interaction effects of bilingualism with the various variables were also calculated by using univariate GLM. Statistical analysis was performed using SPSS 20.0 for Windows software (SPSS Inc., Chicago, IL) and significance was set at p < 0.05.

**RESULTS** General characteristics of the patients with dementia. The study cohort consisted of 648 patients and the men/women ratio was 424:224. The mean age of the group at presentation was 66.2 years (range 32–92 years) and the duration of symptoms ranged from 6 months to 11 years (mean 2.3 years; SD 1.8 years). AD was diagnosed in 240 (37.0%), VaD in 189 (29.2%), FTD in 116 (17.9%), DLB in 55 (8.5%), and mixed dementia in 48 (7.4%). Five hundred fifty patients (85.9%) were literate and 26% were from rural areas.

**Comparison of monolingual and bilingual patient groups.** Slightly more than half of the patients (391, 60.3%) were bilingual, of whom 26.2% spoke 2 languages, 25.0% spoke 3 languages, and 9.1% spoke 4 or more languages. AD dementia, FTD, DLB, and mixed dementia were equally frequently encountered in both of the groups, while the proportion of patients with DLB was higher among bilinguals compared with monolinguals. Severity of dementia measured by ACE-R and CDR was higher among monolinguals. There was no difference in duration of illness, family history of dementia, and vascular risk factor profile between the 2 groups (table 1).

On comparing bilingual with monolingual cohorts, bilinguals were found to be 4.5 older at the time of occurrence of the first symptoms of dementia: 65.6 years in bilinguals as opposed to 61.1 years in monolinguals. A significant difference was found not only comparing all dementia patients, but also within the 3 main

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Table 1	Demographic and clinical characteristics of monolingual and bilingual patients with dementia				
		Monolingual (n = 257)	Bilingual (n = 391)	p Value	
Sex, male		131 (51.0)	293 (74.9)	<0.0001	
Literacy		177 (68.9)	373 (95.4)	< 0.0001	
Years of education		$5.9\pm5.1$	$12.9\pm4.9$	< 0.0001	
Occupation <sup>a</sup>					
Elementary		8 (7.5)	5 (1.9)	0.030	
Skilled workers, clerks		93 (86.9)	177 (68.9)	0.205	
Associate professionals		5 (4.7)	21 (8.2)	0.377	
Professionals		1 (0.9)	54 (21.0)	< 0.0001	
Urban <sup>b</sup>		135 (61.0)	292 (82.2)	< 0.0001	
Age at presentation, y		63.4 ± 11.4	68.1 ± 10.0	< 0.0001	
Age at onset, y		61.1 ± 11.4	65.6 ± 10.0	<0.0001	
Duration of illness, y		2.1 ± 1.7	2.3 ± 1.9	0.124	
MMSE score		16.7 ± 7.5	18.9 ± 8.0	0.0002	
ACE-R		48.6 ± 23.3	55.5 ± 24.7	0.0004	
CDR					
Mild		162 (63.0)	287 (73.4)	0.256	
Moderate		82 (31.9)	84 (21.5)	0.029	
Severe		13 (5.0)	20 (5.1)	0.887	
Dementia su	ıbtype				
AD dementia		98 (38.1)	142 (36.3)	0.806	
FTD		49 (19.1)	67 (17.1)	0.671	
VaD		87 (33.8)	102 (26.1)	0.138	
DLB		7 (2.7)	48 (12.3)	<0.0001	
Mixed		16 (6.2)	32 (8.2)	0.475	
Family history of dementia <sup>c</sup>		36 (14.5)	64 (16.9)	0.565	
Vascular risk factors <sup>d</sup>					
Hypertens	lion	146 (58.4)	214 (55.9)	0.791	
Diabetes		82 (32.8)	132 (34.5)	0.823	
Smoking		35 (14.0)	49 (12.8)	0.791	
Alcoholism		30 (12.0)	50 (13.0)	0.823	
Coronary artery disease		32 (12.8)	75 (19.6)	0.075	
Stroke		69 (27.6)	92 (24.0)	0.493	

Abbreviations: ACE-R = Addenbrooke's Cognitive Examination-revised; AD = Alzheimer disease; CDR = Clinical Dementia Rating; DLB = dementia with Lewy bodies; FTD = frontotemporal dementia; MMSE = Mini-Mental State Examination; VaD = vascular dementia. Data are mean  $\pm$  SD or n (%).

<sup>a</sup> Monolinguals n = 107, bilinguals n = 257, missing data n = 147 (housewives n = 137, excluded from occupational status analysis).

<sup>b</sup> Monolinguals n = 221, bilinguals	n = 355, missing data n = 72
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<sup>c</sup> Monolinguals n = 248, bilinguals n = 378, missing data n = 22.

 $^{d}$ Monolinguals n = 250, bilinguals n = 383, missing data n = 15.

dementia subtypes: a 3.2-year delay in subjects with AD dementia, 6.0-year delay with FTD, and 3.7-year delay with VaD. The difference in age at onset between bilingual and monolingual DLB and mixed dementia was 2.3 and 1.4 years, respectively, but did not reach statistical significance (table 2).

In other variables, the bilingual cohort had more men, more literate individuals, higher educational levels, larger number of urban dwellers, and higher skill levels in their occupation compared with monolinguals. Univariate GLM analysis showed that bilingualism was significantly ( $F_{1,458} = 4.89$ , p = 0.027) associated with age at onset of dementia after adjusting for the other variables such as literacy, years of education, sex, dementia subtype, vascular risk factors, stroke, occupational status, rural/urban dwelling, family history of dementia, and dementia severity (CDR, ACE-R).

To assess the effect of interaction between bilingualism and these factors on age at onset of dementia, we used univariate GLM. We found no interaction effects of literacy ( $F_{I,646} = 0.59$ , p = 0.44), years of education ( $F_{I,646} = 1.74$ , p = 0.18), sex ( $F_{I,646} = 2.0$ , p = 0.16), dementia subtype ( $F_{4,643} = 0.65$ , p = 0.62), vascular risk factors ( $F_{I,631} = 0.34$ , p = 0.56), stroke ( $F_{I,631} = 0.60$ , p = 0.44), occupational status ( $F_{3,360} = 0.83$ , p = 0.48), rural/urban dwelling ( $F_{I,574} = 2.06$ , p = 0.15), family history ( $F_{I,624} = 0.26$ , p = 0.61), and dementia severity on the CDR scale ( $F_{3,644} = 0.65$ , p = 0.58) and ACE-R ( $F_{I,646} = 0.55$ , p = 0.57).

Furthermore, we assessed separately the age at onset of dementia in the illiterate cohort only, excluding subjects who had any type of formal education. We found a significant delay of 6 years among illiterate bilingual dementia subjects in comparison to monolinguals (65.0 vs 59.0 years, p = 0.03).

The association between education and age at onset of dementia in the cohort was also studied. The mean age at onset among illiterate subjects was 60.1 years (SD 10.8) and among literate subjects was 64.5 years (SD 10.7), and the difference was significant (analysis of variance,  $F_{1,646} = 13.95$ , p = 0.0002). Univariate GLM analysis, however, showed that education was not independently associated with age at onset of dementia after adjusting for the other variables ( $F_{1,458} = 0.45$ , p = 0.83).

To explore a possible additive effect of number of languages, we examined the differences between subjects who spoke 2 vs 3 vs 4 or more languages and found no significant difference in dementia age at onset between these groups (table 3). On exploring a possible native language effect, we studied age at onset of bilingual patients with dementia who spoke the 3 principal languages of the region (Telugu = 65.6 years, Dakkhini = 63.5 years, and Hindi = 65.2 years) as their native language and found no differences among these 3 groups of subjects.

**DISCUSSION** This is the largest study so far to examine the impact of bilingualism on dementia and to document a significant delay in the age at onset

Table 2 Age at onset of dementia in subtypes of dementia: Comparison   between monolingual and bilingual groups							
		Age at onset of dementia, y					
Dementia subtype	e No.	Monolingual	Bilingual	p Value			
AD dementia	240	65.4 (10.0); 39.5-92.0	68.6 (9.6); 40.0-89.0	0.013			
FTD	116	55.6 (10.5); 31.0-78.0	61.6 (9.0); 39.0-83.0	0.001			
VaD	189	57.0 (10.7); 37.0-84.0	60.7 (9.7); 41.0-86.5	0.012			
DLB	55	66.7 (11.0); 57.0-84.0	69.0 (8.2); 51.0-80.0	0.506			
Mixed dementia	48	70.1 (10.0); 49.0-83.0	71.5 (7.7); 57.0-85.0	0.608			

Abbreviations: AD = Alzheimer disease; DLB = dementia with Lewy bodies; FTD = fronto-temporal dementia; VaD = vascular dementia.

Data are presented as mean (SD); range, unless otherwise stated.

of dementia symptoms in bilingual patients in comparison to monolingual patients. It is the first study to demonstrate a delay in 3 different types of dementia: not only in AD dementia, but also in FTD and

Table 3	Language profile and age at onset of dementia in different language subgroups			
		No.	Age at onset, y	
One language (n = 257, 39.7%)			61.1 (11.4); 31.0-92.0	
Telugu		235		
Dakkhini		8		
Hindi		7		
English		1		
Other languages		6		
Two languages (n = 170, 26.2%)			66.0 (10.5); 39.0-86.5	
Telugu and English		75		
Telugu and Hindi		42		
Hindi and Dakkhini		12		
Hindi and English		9		
Telugu and Dakkhini		4		
Other lang	Other language combinations			
Three langu	ages (n = 162, 25.0%)		65.1 (9.5); 40.0-89.0	
Telugu, Hi	Telugu, Hindi, English			
Hindi, Dak	Hindi, Dakkhini, English			
Telugu, Hindi, Dakkhini		7		
Hindi, English, and others		22		
Other combinations		15		
Four or more languages (n = 59, 9.1%)			66.2 (10.01); 41.0-85.0	
Telugu, Er	nglish, Hindi, and others	18		
Telugu, Er	Telugu, English, Hindi, and Dakkhini			
Telugu, Er	Telugu, English, Hindi, Dakkhini, and others			
Hindi, English, Dakkhini, and others		3		
Other combinations		20		

Data are presented as mean (SD); range, unless otherwise stated. p < 0.0001, 1 language vs 2 languages, 3 languages, 4 or more languages; p not significant, 2 languages vs 3 languages vs 4 or more languages.

VaD. In contrast to previous studies, the bilingual group was drawn from the same environment as the monolingual one and the results were therefore free from the confounding effect of immigration. The bilingual effect on age at dementia onset was shown independently of other potential confounding factors, such as education, sex, occupation, cardiovascular risk factors, and urban vs rural dwelling, of subjects with dementia. Importantly, for the first time, the bilingual effect was also observed within the illiterate population, demonstrating that bilingualism effects cannot be reduced to differences in education. The observed effects were independent of the specific language spoken. The delay in onset of dementia was almost identical to that reported in previous studies: 4.5 years. Taken together, our results offer strong evidence for the protective effect of bilingualism against dementia in a population radically different from populations studied so far regarding their ethnicity, culture, and patterns of language use.

Interestingly, we could not reproduce the beneficial effect of the number of languages spoken, as advocated in previous studies.2 In our cohort, knowing 3 or more languages did not confer an additional advantage over 2 languages. However, this apparent contradiction could be resolved by considering the differences in several individual and interactional factors related to the pattern of language acquisition, proficiency, and use among different countries. The individual factors include language-learning histories, whether the 2 languages were learned in an informal naturalistic context or whether some languages were learned in formal settings, and whether any one of the various languages was dominant or used more often. The interactional factors include the specific context in which languages were used, the linguistic abilities and preferences of people communicating, and degree of relatedness of the languages, which in turn affects translatability and encoding difficulty or ease.<sup>19</sup>

Following the influential model of Green<sup>20</sup> (1998), language switching has been considered as central in establishing the cognitive advantages of bilingualism. The constant need in a bilingual person to selectively activate one language and suppress the other is thought to lead to a better development of executive functions and attentional tasks with cognitive advantages being best documented in attentional control, inhibition, and conflict resolution.7,8,21 In places in which an official dominant language coexists with a number of minority languages, it can be reasonably assumed that the amount of language switching between languages is proportional to the number of languages spoken: the more languages people know, the more occasion they will have to switch between them. In the strongly trilingual environment of Hyderabad with Telugu, Dakkhini, and English

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being used extensively and interchangeably in both formal and informal environments,<sup>11</sup> with high levels of code switching and mixing,<sup>12</sup> it could be speculated that those speaking 2 languages have already reached a maximum level of switching and the knowledge of additional languages will not be able to increase it. Such an interpretation would be supported by the view that neural mechanisms underlying cognitive control demands in bilingual communities with high levels of code switching are different from bilingual communities with practice in avoiding language switching or mixing.<sup>22</sup>

The effect of attention could also explain the fact that a bilingual advantage was found across different dementia subtypes. Although different forms of dementia have characteristic cognitive profiles, such as episodic memory loss in AD dementia or behavioral impairment in FTD, attentional and executive deficits are common in the early stages of all dementias. Speed of attentional switching and inhibition are found to be impaired in early AD dementia,<sup>23</sup> FTD and VaD are characterized by prominent executive dysfunction,<sup>24,25</sup> whereas DLB is characterized by prominent attentional control deficits.<sup>26</sup> The delay in initial symptom onset in bilinguals across dementia subtypes may therefore be related to the protection from decline of attention and executive functions, as observed in normal aging. The fact that we did not find a significant difference between bilingual and monolingual dementia patients with DLB and mixed dementia does not exclude a potential impact of bilingualism, given the fact that there was a trend toward delay and the size of the 2 groups was small and therefore did not allow detection of subtle differences. Further research is needed to address this question.

Several lifetime experiences such as education, occupation, intellectually stimulating activities, physical exercise, and socioeconomic status have been found to delay the age at onset of dementia by improving "cognitive reserve."5,27,28 One of the main criticisms directed toward studies claiming a relationship between dementia onset and bilingualism is the effect of potential confounding factors, making it difficult to trace any possible genuine effect of bilingualism. Education has been widely studied, but the results so far have been contradictory: in some studies, education could explain the bilingual advantage, in others it could not.<sup>1,2,29</sup> In our study, although bilinguals were overall more educated than monolinguals, the bilingual effect was shown to be independent from education. Moreover, a significant bilingual delay was demonstrated in the group consisting entirely of illiterate patients without any formal schooling. Similarly, other factors that were unequally distributed between the monolingual and bilingual groups (occupational status, male sex, urban dwelling) did not show a significant interaction with

bilingualism. Finally, in contrast to most previous studies, our cohort consisted almost entirely of people who grew up in the Hyderabad area and the state of Andhra Pradesh, minimizing the influence of migration as a confounding variable.

Our study has some limitations. First, age at onset of dementia was determined based on the reports from patients' family members in a clinical setting, and therefore could not be validated. However, because the same criterion was applied to all patients, a systematic bias affecting the results is less likely. Second, similar to most studies examining the relationship between bilingualism and the onset of dementia,<sup>1-3</sup> the definition used for bilingualism was a subjective rating. Objective methods of assessing proficiency in languages were not used. Third, a selection bias might have occurred because all of the patients were those reporting at the specialist clinic and not from the community. This is reflected in the age at onset of our cohort, which was nearly a decade less than reported from epidemiologic studies in India,<sup>30,31</sup> although consistent with Indian memory clinic studies.16,32 Sociocultural protection of elderly and higher levels of comorbidities leading to lower referral rates of elderly, and younger demographic profile due to lower life expectancy,33 are likely to have accounted for this finding. Finally, in the absence of information on how each bilingual patient acquired all the languages they knew, it was not possible to make comparisons based on language combinations.

The converging evidence from different research groups, countries, and cultures, all pointing to bilingualism as a potential protective factor against dementia, makes it increasingly less likely that the bilingualism effect can be reduced to artifacts and confounds. Further studies are needed to substantiate the claim and elucidate the possible neural mechanisms. There is a need for a prospective study, collecting medical, cognitive, linguistic, and social information, ideally in combination with neuroimaging. The linguistic data to be collected should include more comprehensive information about the language acquisition and proficiency. However, what we consider to be most important is the need for comparative studies in different countries, languages, and cultures. Our study demonstrates that investigating a new population with a different pattern of variables associated with bilingualism can unearth insights that would be difficult to obtain by limiting the research to previously studied populations. We hope that our research will stimulate interest in the interactions of bilingualism, cognition, and dementia across the world.

#### AUTHOR CONTRIBUTIONS

Suvarna Alladi contributed to study conception and design, literature search, subject recruitment, data collection, analysis and interpretation, writing of the manuscript. Thomas H. Bak contributed to study conception and design, literature search, data interpretation, writing of the manuscript. Vasanta Duggirala and Bapiraju Surampudi contributed to literature search, data interpretation, editing of manuscript. Mekala Shailaja contributed to literature search, data collection, analysis and interpretation, writing of the manuscript. Anuj Kumar Shukla contributed to literature search, data analysis and interpretation, writing of the manuscript. Jaydip Ray Chaudhuri and Subhash Kaul contributed to study design, subject recruitment, data interpretation, editing of the manuscript.

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#### DISCLOSURE

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