Multilingualism (But Not Always Bilingualism) Delays the Onset of Alzheimer Disease: Evidence From a Bilingual Community

Howard Chertkow, MD, FRCP (C),†‡§‖ Victor Whitehead, MA,* Natalie Phillips, PhD,*¶ Christina Wolfson, PhD,†‖# Julie Atherton, PhD,# and Howard Bergman, MD*†*

Abstract: A recent paper by Bialystok et al in Neuropsychologia (vol. 45, pgs. 459 to 464) suggested that early bilingualism produced a statistically significant 4.1-year delay in onset of memory loss symptoms in older individuals with Alzheimer disease, possibly reflecting an increase in the cognitive reserve of these individuals. That study focused on multilingual elderly patients of whom 90% were immigrants. Our memory clinic, in Montreal Canada, has the advantage of having a large set of individuals who are either multilingual immigrants to Canada, or who are nonimmigrants but raised in both official languages of Canada—French and English. We thus attempted to replicate the above findings using a larger cohort in a different setting. We examined age at diagnosis of Alzheimer disease and age at symptom onset for all unilingual versus multilingual participants, and then for those who were nonimmigrant English/French bilinguals. Overall, we found a small but significant protective effect of more than 2 languages spoken, but we found no significant benefit in bilinguals overall in relation to age at diagnosis or age at symptom onset. However, in the immigrant group, the results mirrored those of Bialystok et al with 2 or more languages delaying the diagnosis of Alzheimer disease by almost 5 years. A trend toward the same effect was also seen in nonimmigrants whose first language was French. In contrast, in nonimmigrants whose first language was English, no such effect was found. These results are discussed in relation to the earlier findings and the theory of cognitive reserve.

Key Words: bilingualism, Alzheimer disease, memory loss, diagnosis, cognitive reserve

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From the §Research Centre, Institut Universitaire de Gériatrie; ‖Department of Neurology and Neurosurgery; *Bloomfield Centre for Research in Aging, Lady Davis Institute for Medical Research, and Jewish General Hospital/ McGill University Memory Clinic, Jewish General Hospital; †Division of Geriatric Medicine, Department of Medicine, McGill University; ‡Department of Clinical Neurosciences, Sir Mortimer B. Davis -Jewish General Hospital; ¶Department of Psychology/Centre for Research in Human Development, Concordia University, Montreal, Qubec, Canada; and #Department of Epidemiology and Biostatistics and Occupational Health, McGill University; Division of Clinical Epidemiology, McGill University Health Centre.

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Reprints: Howard Chertkow, MD, Bloomfield Centre for Research in Aging, Lady Davis Institute for Medical Research, and Jewish General Hospital/McGill University Memory Clinic, Jewish General Hospital, McGill University, Montreal, Quebec, Canada, H3T-1E2 (e-mail howard.chertkow@mcgill.ca).

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Several recent studies have presented evidence regarding "cognitive reserve" protective factors in Alzheimer disease (AD) and there is growing evidence that a number of environmental and life factors enhance cognitive reserve, and possibly protect against dementia and AD.[1,2] Daily mental activities were associated with a significant relative risk reduction in the Kungsholmen Study.[3] In the Washington Heights District of New York, a longitudinal study found an inverse association between leisure activities and the incidence of dementia.[4] Higher levels of education have been associated with reduced risk of AD, and this relationship has been confirmed across centers.[5] Thus, the suggestion has been made that a sustained high level of complex mental activity protects against dementia.[6,7] These authors suggest that the effects of such activity might be to build reserve and therefore delay (but not necessarily prevent) the onset of dementia owing to AD. The mechanisms of cognitive reserve are the subject of recent investigations, and possible mechanisms include physiologic alterations such as enriched cerebral vascular supply and increased neuronal connections, along with better use of additional brain regions for compensation.[8]

A recent study [9] explored the possibility that bilingualism builds cognitive reserve and that this is reflected in a delay in onset of dementia. Bialystok et al earlier showed that lifelong bilingualism conferred cognitive advantages in terms of better attention and cognitive control in children and adults.[10–12] This led to the hypothesis that "bilingualism might contribute to cognitive reserve and protect older adults from decline in the context of dementia."[9] Bialystok et al sought to confirm this hypothesis by examining data on age of onset of memory complaints and bilingualism in a cohort of 184 individuals in Toronto, Canada. Participants included 132 individuals with a diagnosis of probable AD, and 52 individuals with possible AD, mixed, cerebrovascular, or other dementia. Ninety-one of the 184 were judged to be unilingual (90% being born in Canada), and 93 were bilingual. More than 90% of the bilingual participants were immigrants who had arrived in Canada in the 1940s to 1960s. Families were asked to judge the age of onset of the patient's memory problems. The average age of reported memory impairment onset (based on this method of assessment) was 71.4 years in the unilingual group, and 75.5 years in the bilingual cohort, a statistically reliable difference. The authors concluded that bilingualism had conferred a protective effect by delaying the onset of memory loss by about 4.1 years on average and argued that no other cultural factors could account for the group differences.

Bialystok is not entirely alone in her conclusions. A recent poster by Montoya et al[13] reached a similar conclusion in a group of 37 Spanish/English bilinguals. Kavé et al[14] found evidence of better cognitive function in the nondemented elderly in Israelis as a function of the number of languages spoken (2, 3, or more), irrespective of education level.

We consider these results to be potentially important, and that they require replication. One concern is that there may have been several confounding factors that were not taken into account in the analysis. First, there was a mixture of diagnoses of dementia, making it difficult to know if the effect of bilingualism is specific to AD. Second, we are concerned about the reliance on an estimated measure of age of memory impairment onset, a notoriously unreliable measure for families to provide, which can introduce information bias.[15] Third, we are most concerned that the 2 "language" cohorts are quite different, with 1 being elderly immigrants and the comparison group being unilingual individuals most of whom spent much of their lives in Toronto. The life experiences of the immigrants (who were for the most part children and teenagers who lived in Europe during World War II) likely differ from the Canadians in unmeasured ways in terms of diet, stress, and life history, all of which are possible risk factors related to the timing onset of dementia. Although common sense suggests that the nonimmigrant cohort should have the advantages, this might not necessarily be the case. For example, there are animal studies in which nutritional deprivation produced a delay in brain aging and decreased brain oxidative stress[16,17] and there are human studies showing caloric restriction improves memory in the elderly.[18]

For these reasons, we have taken advantage of the bilingual nature of Montreal to attempt to replicate the findings of Bialystok et al. In Montreal, among seniors, many individuals were born locally and spoke only English or French during their youth and even into their adult life. Other individuals, also born in Montreal, grew up speaking both English and French. Finally, there are also immigrants who acquired a different birth language abroad. In our view, these are natural comparison groups as it is reasonable to assume that those born in Montreal had very similar life and cultural experiences, allowing for a more controlled comparison between bilinguals and monolinguals.

METHODS

The database of the Memory Clinic of the Jewish General Hospital in Montreal, Canada, a tertiary care referral clinic, contains information on 1842 individuals referred between 1997 and 2006. For the purposes of this research, we restricted our sample to those 632 individuals with memory complaints who were subsequently diagnosed with probable Alzheimer dementia (AD). AD was diagnosed by a neurologist or geriatrician in consultation with other Memory Clinic physicians, nurses and neuropsychologists using National Institute of Neurological and Communicative Disorders and Stroke- the Alzheimer's Disease and Related Disorders Associationcriteria.[19] The diagnosis of dementia was, for most patients, made at the time of the first visit to the Memory Clinic. The initial diagnosis was Mild Cognitive Impairment (MCI) for 130 participants, and annual follow-up visits were carried out. For these 130 individuals, the date of onset of dementia was defined as the clinic visit at which the diagnosis was changed from MCI to AD. In a subset of all of the dementia cases, follow-up occurred a year after the diagnosis was given. Folstein mini-mental state examination (MMSE)[20] scores were available for both the initial diagnostic visit and the annual follow-up visit.

In this study , we have information on age at the time of their initial diagnosis for all patients. Age of symptom onset information was formally assessed in a subset of 143 patients, consisting of family interviews in which an estimate of the year and month of onset of memory complaints was determined by asking the question "Can you give the month and year when you first noticed memory problems (in the patient)."

Language history was obtained from patient and caregiver interviews. We defined 3 levels of language ability: unilingual, bilingual, and multilingual. The definitions of these levels changed slightly depending on the analysis being done. Unilingual participants spoke only 1 language. For our comparisons of those speaking 1 versus multiple languages, multilingual participants were defined as speaking 2 or more languages. For analyses of the effects of increasing numbers of languages spoken, bilingualism was defined as speaking 2 languages, whereas multilingualism in that case was defined as speaking 3 or more languages. For our analysis of bilingualism in our nonimmigrant population, we considered only those who spoke both French and English (but not other languages) since youth as the "bilingual" cohort for that analysis, and our unilingual cohort was made up similarly of English and French speakers only. Bilingualism/multilingualism was defined according to the criterion set out by Bialystok et al for bilingualism ("The criterion for bilingualism was that patients had spent the majority of their lives, at least from early adulthood, regularly using at least two languages" p. 460[9]). We did not control specifically for the age at which the second language was learned.

We did not have direct information on immigrant/native status for our patients and therefore made a rough approximation based on the assumption that all patients whose first language was English or French (Canada's official languages) or one of Canada's aboriginal languages (eg, Mohawk—only 1 patient met this criterion) were born and/or primary/secondary school-educated in Canada (henceforth native), whereas all unilingual speakers of languages other than English or French and all multilingual speakers whose first language was neither English or French were born and/or primary/secondary school-educated outside of Canada (henceforth immigrants). In our sample, there were 253 "multilinguals" [135 (53%) of whom were defined as immigrants] and 379 unilinguals [23 (6%) of whom were defined as immigrants] of which 66 (17%) spoke only French whereas 290 (77%) spoke only English (see Table 1 for an overview of the breakdown of our cohort, and supplementary materials for a fuller description of our cohort). As we did not have direct information on immigrant status, we could not determine age of immigration.

Socioeconomic status (SES) of participants was assessed retrospectively by applying the method outlined in Bialystok et al using occupation status as a proxy for SES (see supplemental materials for a full description http://links.lww.com/WAD/A2).

RESULTS

Overall Impact of Bilingualism or Multilingualism on Age of Diagnosis of AD

The mean values for age at diagnosis, years of education and MMSE score at diagnosis for the cohort

TABLE 1. n of Cohort and its Breakdown According to Immigrant Status, Language Status, and, for the Native Groups, English /French (E/F) Bilingualism

Total n of Cohort	632
N of nonimmigrant (Canada born/educated) subgroup*	474 (75%)
N of nonimmigrants whose first language was English	379
n who were unilingual	290
n who were bi- or multilingual	89
n who were E/F bilingual	19
N of nonimmigrants whose first language was French	94
n who were unilingual	66
n who were bi- or multilingual	28
n who were E/F bilingual	24
N of immigrant subgroup	158 (25%)
n who were unilingual	23
n who were bi- or multilingual	135

*One nonimmigrant subject spoke Mohawk as a first language and was thus not included in either the nonimmigrant English or nonimmigrant French subgroups.

are reported in Table 2. A cross-tabulation of sex and language group showed a significant difference in distribution of men versus women in each language group with women being far more represented in the unilingual group than in the multilingual group (Pearson chi square = 8.3, $P < 0.01$). There was also a trend toward men being diagnosed at a later age than women overall, $z = 1.66$, $P < 0.097$. According to our definitions, the cohort was made up of 158 immigrants (25%) and 474 natives (75%). There was no difference in age of diagnosis between the 2 groups, $z = 0.96$, $P = 0.34$. A cross-tabulation of immigrant/native status and language group showed natives to be far more likely to be unilingual than immigrants ($\chi^2 = 178.2$, $P < 0.001$). A cross-tabulation of sex and immigrant/native status showed no difference in the distribution of women and men in each group ($\chi^2 = 1.04$, $P = 0.31$). Immigrants had significantly less years of education than natives, however, (9.7 vs. 11.2, $z = 4.5$, $P < 0.001$). There was no difference between unilinguals and multilinguals in years of education (10.9 vs. 10.7, $P > 0.05$) and there was no correlation between education and age of diagnosis ($r = 0.05$, $P = 0.26$, 95% CI = -0.03-0.12).

Given the potentially confounding impact of sex, immigrant/native status, and education on our data, we elected to do regression analyses on our variables of interest with education, immigrant/native status and sex as covariates with language status. In the cases where a variable was categorical [eg, sex (male/female)], the numbers 0 and 1 were used to code the alternate states.

A model regressing age of diagnosis to language status (unilingual vs. multilingual), education, immigrant/native status, and sex trended toward but did not reach significance overall [$F(4, 627) = 2.02$, $P = 0.09$] and 2 of the independent variables in the model contributed to that trend [language status: unstandardized β coefficient (uβc) = 1.40, $P = 0.06$; immigrant/native status: uβc = -1.43, $P = 0.09$] whereas the other 2 did not (education: uβc = 0.06, $P = 0.45$; sex: uβc = 0.83, $P = 0.18$) (see Table 2). Given that language status trended toward significance, we further examined whether the number of languages spoken within the multilingual group had an impact on diagnosis. Among multilinguals, the number of languages spoken was found to have a small but significant positive association with age at diagnosis (Spearman $r = 0.14$, $P = 0.026$ (95% CI for $r = 0.02$-0.26)], suggesting the more languages spoken, the later dementia was diagnosed. To further examine this association, we did a multiple regression analysis looking at the relation of the number of languages spoken with age of diagnosis in multilinguals in addition to education, immigrant/native status and sex. The overall model trended toward significance [$F(4, 248) = 2.2$, $P = 0.07$]. Of the individual variables, only the number of languages came out as a significant predictor (uβc = 1.90, $P = 0.008$), whereas education, immigrant/native status and sex did not significantly contribute to the model (education: uβc = -0.04, $P = 0.72$; immigrant/native status: uβc = -0.94, $P = 0.32$ sex: uβc = 0.79, $P = 0.39$). A post hoc least significant difference analysis of the different groups based on number of languages spoken (2, 3, or 4+) showed that those who spoke 4 or more were diagnosed significantly later than those who spoke only 2 (Mean difference = 4.19, $P = 0.02$), whereas those who spoke 3 languages showed a trend toward later diagnosis than those who spoke 2 (Mean difference = 1.87, $P = 0.075$). Including the unilinguals in the model made the regression significant [$F(4, 627) = 3.7$, $P = 0.006$]. The individual variables that came out as significant was a positive relationship with the number of languages (uβc = 1.4, $P = 0.001$) and a negative relationship with immigrant status (uβc = -2.0, $P = 0.017$), suggesting that the more languages spoken delayed time of diagnosis of AD, whereas being an immigrant hastened it. Education and sex did not contribute significantly to the model (education: uβc = 0.06, $P = 0.49$; sex: uβc = 0.71, $P = 0.25$). In this case, the post hoc LSD analysis of number of languages showed a significant difference in age of diagnosis between those who spoke 4 or more languages and those who spoke 1 (mean difference: 4.21 y, $P = 0.02$) or 2 languages (mean difference: = 4.19 y, $P = 0.02$) and a trend for those who spoke 3 languages versus those who spoke 1 (mean difference = 1.89 y, $P = 0.06$) or 2 languages (mean difference = 1.87 y, $P = 0.09$). There was no difference between those who spoke 1 or 2 languages (mean difference = 0.02 y, $P = 0.98$). These results suggest that speaking 3 or more languages is protective, but that speaking only 2 is not (see Table 3).

TABLE 2. Mean Values (and Standard Deviation) for Demographic Variables of Each Language Group

Language Group	n	Age at Diagnosis Mean (SD)	Years of Education Mean (SD)	MMSE score Mean (SD)
Unilingual	379	76.7 (7.8)	10.9 (3.5)	23.1 (3.9)
Men	139	77.1 (7.0)	11.1 (3.7)	22.7 (4.0)
Women	240	76.3 (8.1)	10.8 (3.3)	23.3 (3.8)
Multilingual	253	77.6 (7.2)	10.7 (3.8)	22.9 (4.3)
Men	122	78.1 (7.3)	11.1 (4.2)	23.5 (4.3)
Women	131	76.9 (7.5)	10.3 (3.4)	22.4 (4.2)

Impact of Bilingualism or Multilingualism on Age of Symptom Onset

In 143 participants, we had available a detailed assessment to attempt to determine the month and year of onset of memory impairment symptoms. This consisted

TABLE 3. Demographic Information Organized According to Number of Languages Spoken

Number of Languages Spoken	n	Age at Diagnosis	Years of Education	MMSE Score at Diagnosis
1	379	76.7 (7.8)	10.9 (3.5)	23.1 (3.9)
2	168	76.7 (7.8)	10.7 (3.7)	22.8 (4.3)
3	67	78.6 (6.0)	11.3 (4.2)	23.1 (4.3)
≥ 4	18	80.8 (5.5)	9.1 (3.6)	23.6 (2.7)

of detailed questioning based on the CSHA approach.[15] This group of 89 unilinguals and 54 multilinguals, was re-analyzed separately. Z-tests were carried out to compare this subset of 143 patients to the rest of the sample on age of diagnosis, education, number of languages, and MMSE score at diagnosis. No difference was found in education (10.8 vs. 10.8, $P = 0.86$) or number of languages (1.5 vs. 1.6, $P = 0.47$). Differences were found in age and MMSE score at diagnosis, with the subset being younger and having a higher MMSE score on average (mean age: 75.9 vs. 77.3, $P < 0.05$; mean MMSE score, 23.8 vs. 22.8, $P < 0.01$). As in Bialystok et al,[9] we examined the time between symptom onset and first assessment as a function of immigrant status to check for a potential confound of individuals being less inclined to present themselves for medical help as a result of being from different backgrounds. We found no difference between immigrants and native-born Canadians on this measure [time from symptom onset to first assessment: immigrants = 4.5 y; native born Canadians = 4.8 y; $F(1, 141) = 0.15$, $P = 0.7$]. A model regressing age of diagnosis to language status (unilingual vs. multilingual), education, immigrant/native status and sex was not significant overall in this subgroup [$F(4, 138) = 0.43$, $P = 0.79$] and neither were any of the individual variables in the model (language status: uβc = 1.76, $P = 0.25$; immigrant/native status: uβc = -1.49, $P = 0.36$; education: uβc = -0.01, $P = 0.97$; sex: uβc = -0.545, $P = 0.67$). A similar analysis of age of symptom onset also did not show a difference [$F(4, 138) = 0.57$, $P = 0.68$; language status: uβc = 1.93 $P = 0.23$, immigrant/native status: uβc = -2.13, $P = 0.24$, education: uβc = 0.02, $P = 0.89$, gender: uβc = -0.14, $P = 0.92$]. A correlation of age of onset of memory problems with number of languages spoken among the multilinguals showed a positive relationship as in the larger group with age of diagnosis (Spearman $r = 0.32$, $P < 0.02$, 95% CI for $r = 0.05$-0.54). A further regression analysis of this effect in the presence of education, immigration/native status and sex gave the subsequent result: the overall model was not significant [$F(4,138) = 1.7$, $P = 0.15$], but number of languages was (uβc = 2.4, $P = 0.02$) and immigrant/native status trended toward significance (uβc = -3.2, $P = 0.06$). A post hoc LSD analysis of 1 versus 2 versus 3 + languages spoken (4, & 5 were combined with 3 owing to smaller numbers in this subgroup) showed those who spoke 3 or more languages had a later onset of symptoms than those who spoke 1 (mean difference = 4.84 y, $P = 0.026$) or 2 languages (mean difference = 5.47 y, $P = 0.022$). As with age of diagnosis, there was no significant difference between those who spoke 1 or 2 languages, although unilinguals' average symptom onset was slightly later than bilinguals (mean difference = 0.63 y, $P = 0.68$). These results mirror the age of diagnosis results (see supplementary materials for a table of the demographics of the age of onset subcohort).

Analysis of Impact of English-French Bilingualism in Nonimmigrant Cohort on Age of Diagnosis of AD

One of the motivations for this study was to look at the effect of bilingualism without the potential confound of differences in cultural and life experience between individuals born in Canada and individuals who were immigrants. To that end, we carried out a further analysis essentially restricted to Canadian born participants. We assessed the subgroup of individuals who were unilinguals in either English or French, comparing them to the French/English bilinguals. These individuals were almost all born in or around Montreal. This group was made up of 356 unilinguals (290 English-speaking, 66 French-speaking) and 43 bilinguals (19 with English as first language and 24 with French as first language). The unilinguals were 81% English speaking compared with only 19% French speaking. In this group, a regression model for age of diagnosis with bilingualism status (unilingual vs. bilingual), education, and sex did not reach significance overall [$F(3, 394) = 2.02$, $P = 0.11$]. The subvariable for bilingualism did, however, reach significance (uβc = -3.0, $P = 0.018$). When we examine the means, however, the difference turns out to be in favor of the unilinguals being diagnosed later than the bilinguals (see supplementary materials for a table of demographics of the native English/French unilinguals and bilinguals).

Further analysis of the groups according to the first language showed that among the unilinguals, French speakers were diagnosed on average 5.3 years earlier than English speakers (72.7 vs. 78.0; $z = 4.5$, $P = 0.0001$), whereas in the bilinguals there was no difference [French = 75.9, English = 73.2; $t(\text{df} = 41) = 1.02$, $P = 0.32$]. We then looked the larger native English and French group, including speakers of more than 2 languages and bilinguals who spoke additional languages other than English or French. Examining language status within each group, we found there was no difference in the age of diagnosis for the native English group based on number of languages spoken when controlling for education and gender (uβc = 0.51, $P = 0.54$), whereas in the native French group, there was a trend toward significance (uβc = 3.4, $P = 0.084$). Looking only at bilinguals versus unilinguals in the native French group, the difference did not reach significance [$t(\text{df} = 88) = 1.6$, $P = 0.12$] (see Table 4). This suggests that in the native

TABLE 4. Age of Diagnosis of Alzheimer's Disease Organized According to Number of Languages Spoken Within Native Canadians Whose First Language is English (Native English), Native Canadians Whose First Language is French (Native French), and Immigrants to Canada (Immigrants)

Number of Languages Spoken	Native English	Native French	Immigrants
1	78.0 (7.0)	72.7 (9.1)	71.4 (8.1)
(n)	(290)	(66)	(23)
2	77.9 (7.5)	75.9 (6.5)	76.5 (8.2)
(n)	(62)	(24)	(81)
3	79.8 (5.6)	79.5 (2.5)	77.8 (6.4)
(n)	(24)	(4)	(39)
≥ 4	80.7 (3.2)	—	80.9 (5.9)
(n)	(3)	—	(15)

English group, the number of languages spoken did not provide or contribute to a later diagnosis, whereas in the native French population, it trended in that direction, although again at greater than 2 languages.

Analysis of Age of Diagnosis of AD as a Function of Number of Languages Spoken in Immigrant Subgroup

Given the unexpected results we obtained in the native English and French groups, we looked at our immigrant group separately to see if it showed a similar pattern. A model regressing age of diagnosis to language status (unilingual vs. multilingual), education and sex was significant overall in this subgroup [$F(3, 157) = 5.09$, $P = 0.002$] with language status driving the significance (uβc = 4.8, $P = 0.01$). Education and sex did not contribute significantly to the model (education: uβc = 0.21, $P = 0.18$; sex: uβc = 1.4, $P = 0.25$). Replacing simple language status with number of languages (1, 2, 3, 4+) in the regression made for an even stronger model [$F(3,157) = 6.8$, $P = 0.0001$] with number of languages again being significant (uβc = 2.5, $P = 0.001$) and education showing a trend toward significance (uβc = 0.28, $P = 0.055$). Further post hoc analyses showed a significant difference between unilingual immigrants and all other language groups, with unilinguals being diagnosed 5 years earlier than bilinguals ($P = 0.006$), 6.4 years earlier than trilinguals ($P = 0.002$), and 9.5 years earlier than those speaking 4 or more languages. Also, there was a significant difference between 4+ language speakers and bilinguals, with bilinguals being diagnosed 4.5 years earlier on average ($P = 0.038$). A post hoc analysis of education showed unilinguals had significantly less education than all other language groups (6.2 y vs. 10.7, 10.2, 9.0 y for the 2, 3, and 4+ language groups, respectively; *P*s between 0.001 and 0.03) and there were no differences between the other groups. It should be noted that, given our definition of immigrants for this study (first language not English or French), the unilinguals therefore did not speak either of the local languages. In the immigrant subgroup, we see a definite impact of number of languages spoken, both at the level of bilingualism and at the level of 4 or more languages (see Table 4 and supplementary materials for a table of education and MMSE scores by cultural group and linguistic attainment).

Analysis of Age of Diagnosis of AD as a Function of Cultural Group (Native English, Native French, Immigrant) and Number of Languages Spoken

To further examine the patterns uncovered by separating the cohort into Canadian born participants whose first language was English, Canadian born participants whose first language was French, and immigrants, we analyzed the difference in age of diagnosis between these groups within each linguistic group (1 language, 2 languages, etc.). In the unilingual group, there was a significant difference in the age of diagnosis [$F(2, 378) = 20.02$, $P = 0.0001$]. Post hoc LSD analysis showed Canadian born participants whose first language was English were diagnosed significantly older than Canadian born participants whose first language was French (5.36 y, $P = 0.0001$) and immigrants (6.57 y, $P = 0.0001$). There was no significant difference between Canadian born participants whose first language was French and immigrants. In the bilingual and multilingual (3+ languages) groups, there was no significant difference between the 3 groups (bilinguals: [$F(2, 166) = 0.91$, $P = 0.41$]; Multilinguals: [$F(2, 84) = 0.37$, $P = 0.69$]. This shows that native English unilinguals are diagnosed later than either native or immigrant unilinguals, but that this difference disappears in bilinguals and multilinguals.

Analysis of Impact of Occupational Status

Given the difference in age of diagnosis between our native English unilinguals and the other unilinguals, we looked at the possible impact of occupational status in protecting against the onset of dementia in the unilinguals. Higher occupation status and more intellectually stimulating work are associated with retained cognitive function in old age[21,22] and reduced effects of dementia.[23] However, in our cohort, we found that the group with the highest occupational status was the unilingual native French. This shows that the difference seen in the age of diagnosis between native English unilinguals and the other unilinguals is not attributable to occupational status. (see supplementary materials for a table and fuller description of this analysis).

Analysis of Rate of Cognitive Decline

Finally, the rate of cognitive decline after the diagnosis of AD was assessed using Folstein MMSE score at 2 visits, the initial diagnosis visit and the subsequent visit, in a subset of 92 of the unilinguals and 62 of the multilinguals. There was no difference between these rates when regressed with education, immigrant/native status, and gender effects. Our analysis produced rates of decline similar to the results of Bialystok et al[9] (see supplementary materials for a fuller description of this analysis).

DISCUSSION

In this study, we found only partial evidence for a protective effect of bilingualism using 6 different approaches to analysis. On the one hand, we were unable to clearly replicate the results reported by Bialystok et al: whereas they found a statistically significant 4.1-year average difference in age at symptom onset with later onset in the multilingual group, we found a nonsignificant 1.0-year difference between the 2 groups, with multilinguals having symptom onset slightly later. When we considered age of dementia diagnosis rather than age at symptom onset, this difference (still favoring multilingual individuals) was reduced to 0.9 years (see Table 2), and again was found not significant. When we considered age of dementia diagnosis, restricting the cohort to nonimmigrant English/French bilinguals, the difference was now significant, but in the opposite direction, with unilingual individuals having dementia diagnosis 2.6 years later than bilinguals. Furthermore, we found no difference in the rate of cognitive decline between the multilingual and unilingual groups.

In contrast, there was other evidence found favoring a protective effect for multilingualism consisting of a significant relationship between number of languages spoken, and age of diagnosis assessed with Spearman correlation, with those speaking more languages having an older age at diagnosis and symptom onset. A linear regression analysis supported the significance of this finding. Post hoc analysis and examination of Table 3 suggests that this delay in age at diagnosis holds only for men and women speaking 3 or more languages. Further analyses of the native English, native French and immigrant subcohorts showed that bilingualism was significantly protective among immigrants (with bilinguals being diagnosed 5.1 y later than unilinguals), and trended toward significance in our native French subcohort, (with bilinguals being diagnosed 3.2 y later than unilinguals). However, this protective effect was conspicuously absent in our native English subcohort, owing to the linear age of diagnosis present across all language status subgroups. In fact, our uniligual English group was diagnosed at approximately the same age as our multilingual native French and immigrant groups.

These results are fairly straightforward but also perplexing; immigrants and native-born bilinguals whose first language is French show a protective effect of bilingualism (and even more so of multilingualism), whereas native-born bilinguals whose first language is English (ie, the large majority of our cohort) do not show this protective effect. We see the effects solely when these 3 groups are separated out. For all the other analyses, the absence of any protective effect in the native English group serves to "wash out" the effect of number of languages spoken in the entire group, whether we consider age at dementia diagnosis or age at onset of symptoms.

Note that if one considers only the immigrant subgroup in our study (Table 4), the age at dementia diagnosis was remarkably similar to the age of symptom onset found in Bialystok et al, as was the beneficial effect of bilingualism versus unilingualism (although in that study the unilinguals were mostly Canadian born). Although the effect of bilingualism is strongest in our immigrant subgroup, there are also other possible reasons for this finding that our data suggest. First, there is the finding of lower education in our immigrant unilingual group as compared with the bilingual or multlingual immigrants. Lower education has been associated with earlier onset of dementia.[24,25] This could also contribute to their not learning additional languages. As well, given our definition of immigrants as not having as their primary language either English or French, this would mean that unilingual immigrants do not speak either of the main languages of the community. It is possible that this could make them more isolated from the larger community and contribute to greater stress in day to day living, both of which are also associated with earlier onset of dementia.[26,27] Recall that most of the bilingual participants in their study were immigrants, suggesting that the finding does not generalize reliably beyond that population.

The puzzle is why native-born bilingual speakers whose first language is English performed differently. The unilingual English speakers had no evidence of any earlier onset of AD symptoms or diagnosis compared with multilinguals. Owing to their greater age at diagnosis, the data even trended in the opposite direction. When the bilingual group is restricted to Canadian-born French and English speakers, we found some evidence of a later age at diagnosis among unilinguals compared with bilinguals. Given that these groups are better matched and drawn from a more homogeneous background than a sample of patients from immigrant backgrounds, we expected to encounter no differences between English and French native speakers; however, the opposite was the case.

So how do we explain these results? The education levels between the French and English native groups were not different; thus, this factor is unlikely to be responsible. It is documented that prior to the 1960s there was a socioeconomic divide between the English and French populations of Canada, with the English population having greater access to higher paying employment than the French, who made only 62% of the income of the English population according to the 1961 Census.[28] Given that most of our cohort entered the workforce before 1960, we had anticipated a tendency for the unilingual English-speaking native population of the memory clinic from which this group was sampled to have worked in a profession (medicine, law) or to have owned their own business whereas many (although not all) of the French-speaking population were retired laborers. In fact our analysis of occupational status within the unilinguals suggested that the Native French group had a higher occupational status than either the native English group or the immigrants, who were equivalent. We cannot ascribe any cognitive reserve effects, therefore, to differences associated with a higher SES among certain subgroups. If there are environmentally induced differences in cognitive reserve between the English and French subgroups, the source of this remains to be determined.

Alternatively, the English (mostly of British or Eastern European ancestry) and French (mostly of Western European ancestry) subgroups come from differing genetic backgrounds. Might there be certain populations wherein multilingualism produces beneficial "cognitive reserve" whereas other groups fail to gain such a benefit? This is purely speculative. In either case, these data point to the complexity of multiple influences that might affect "cognitive reserve." It seems that the benefit of bilingualism may emerge only if other factors (genetics, socioeconomic status, stress) are equivalent across groups.

We must acknowledge some important limitations of our study. First, we have used a definition of bilingualism and multilingualism that makes no mention of the age of acquisition of the second or other languages or of age of immigration, which has been shown to also have an impact on additional language learning.[29] This was done for practical reasons—it would be quite unreliable to depend on the report of elderly demented individuals as to the exact age at which they acquired a second language. A second limitation was the lack of direct information of immigrant/native status. We used a rough estimation based on the assumption that anyone whose first language was a language native to Canada was native-born, and those whose first language was not native to Canada were immigrants. We understand that it may be argued that some participants in the native category could have immigrated from English-speaking countries or French-speaking countries, and that individuals born in Canada may have a first language other than English or French (ie, if their parents were recent immigrants). We would respond, however, that in the absence of direct information, this method of estimation comes closest to accurately categorizing our cohort in terms of their native/immigrant status and that, in the main, it is correct. A third and fourth limitation was the relatively small sample size of the bilingual native-born cohort, along with the cross sectional nature of the study. Last, a fifth limitation was our use of the age at diagnosis (age of presentation to the clinic, or age at which an MCI individual was rediagnosed as AD) as the main outcome measure in the majority of statistical comparisons. Given the many environmental factors (access to specialists, clinic waiting time) the age at diagnosis is a somewhat arbitrary marker for most individuals. In contrast, there were no obvious systemic factors that should have made the age at diagnosis different for unilingual or bilingual or multilingual individuals and our original hypothesis that immigrants may seek help at a later time was not supported. We can therefore argue that age of diagnosis is a valid evaluation point for the hypothesis that bilingualism delays dementia.

The other analysis was carried out for the age of onset of memory problems, determined in a subset of our participants. Note that "age of onset of memory problems," whereas seemingly a more "ecological" milestone, is also fraught with problems. It has been shown that informants often fail to recognize memory problems in their family members.[30] Recent work by one of us has showed that both of these points in the natural history will be misreported by many participants with memory loss, often by up to a year in either direction.[15] In that study, the reported age of onset of memory problems was in fact a year later than the reported age at which individuals saw a physician for assessment of their memory problems. Again, however, there was no obvious systematic factor that would make unilinguals report an earlier onset age than multilinguals in our study, especially after our original hypothesis that immigrants would be more likely to report later was not supported.

It should be noted that overall our age of symptom onset and diagnosis was considerably younger than the Canadian average determined from data collected 15 years ago in a large population study, the Canadian Study of Health and Aging (CSHA).[31,32] Analysis of the data from 983 CSHA participants showed a mean age of onset of memory problems as 80.5 years, compared with our age of onset of 71.5 years in unilinguals and 72.5 years in multilinguals. This difference may reflect growing public awareness of dementia, or cultural local factors in Montreal, or the fact that those who are older are less likely to present to their physicians or a memory clinic. In contrast, it could simply reflect oversampling of the older age groups in the CSHA.

In summary, these findings both constrain and expand upon the findings of Bialystok et al.[9] On the one hand, we found a protective effect of bilingualism in native Canadians whose first language was French and also in immigrants to Canada, in replication of their results. On the other, this benefit was absent in native English speakers, the majority of our participants, and thus overall, bilingualism did not show a protective effect in our cohort. However, we did find a consistent protective effect for speaking 3 or more languages, both overall and in individual groups, which is consistent with the findings of Kavé et al.[14] Therefore, the protective effect of speaking multiple languages may be clearest in those speaking more than 2. Further research will be needed to clarify these intriguingly different patterns and the meaning of these trends in understanding cognitive reserve.

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REFERENCES

1. Stern Y. What is cognitive reserve? Theory and research application of the reserve concept. *J Int Neuropsychol Soc*. 2002;8:448–460.
2. Scarmeas N, Stern Y. Cognitive reserve and lifestyle. *J Clin Exp Neuropsychol*. 2003;25:625–633.
3. Wang HX, Karp A, Winblad B, et al. Late-life engagement in social and leisure activities is associated with a decreased risk of dementia: a longitudinal study from the Kungsholmen project. *Am J Epidemiol*. 2002;155:1081–1087.
4. Scarmeas N, Levy G, Tang MX, et al. Influence of leisure activity on the incidence of Alzheimer's disease. *Neurology*. 2001;57:2236–2242.
5. Kukull WA, Higdon R, Bowen JD, et al. Dementia and Alzheimer disease incidence: a prospective cohort study. *Arch Neurol*. 2002;59:1737–1746.
6. Valenzuela MJ, Sachdev P. Brain reserve and cognitive decline: a non-parametric systematic review. *Psychol Med*. 2006;36: 1065–1073.
7. Valenzuela MJ, Sachdev P. Brain reserve and dementia: a systematic review. *Psychol Med*. 2006;36:441–454.
8. Fratiglioni L, Paillard-Borg S, Winblad B. An active and socially integrated lifestyle in late life might protect against dementia. *Lancet Neurol*. 2004;3:343–353.
9. Bialystok E, Craik FI, Freedman M. Bilingualism as a protection against the onset of symptoms of dementia. *Neuropsychologia*. 2007;45:459–464.
10. Bialystok E. *Bilingualism in Development: Language, Literacy, and Cognition*. New York: Cambridge University Press; 2001.
11. Bialystok E, Craik FI, Klein R, et al. Bilingualism, aging, and cognitive control: evidence from the Simon task. *Psychol Aging*. 2004;19:290–303.
12. Bialystok E, Craik FI, Ryan J. Executive control in a modified antisaccade task: effects of aging and bilingualism. *J Exp Psychol Learn Mem Cogn*. 2006;32:1341–1354.
13. Montoya RI, Gollan TH, de Pena E, et al. Does Bilingualism Delay Alzheimer's Disease Onset? Evidence from a Hispanic Cohort. Paper presented at: International Neuropsychological Society 36th Annual INS Meeting, 2008; Waikoloa, Hawaii, USA.
14. Kavé G, Eyal N, Shorek A, et al. Multilingualism and cognitive state in the oldest old. *Psychol Aging*. 2008;23: 70–78.
15. Rouah F, Wolfson C. A recommended method for obtaining the age at onset of dementia from the CSHA database. *Int Psychogeriatr*. 2001;13(supp 1):57–70.
16. Masoro EJ. Subfield history: caloric restriction, slowing aging, and extending life. *Sci Aging Knowledge Environ*. 2003;2003: RE2.
17. Matochik JA, Chefer SI, Lane MA, et al. Age-related decline in striatal volume in rhesus monkeys: assessment of long-term calorie restriction. *Neurobiol Aging*. 2004;25:193–200.
18. Witte AV, Fobker M, Gellner R, et al. Caloric restriction improves memory in elderly humans. *Proc Natl Acad Sci USA*. 2009;106:1255–1260.
19. McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*. 1984;34:939–944.
20. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatric Res*. 1975;12:189–198.
21. Staff RT, Murray AD, Deary IJ, et al. What provides cerebral reserve?. *Brain*. 2004;127:1191–1199.
22. Garibotto V, Borroni B, Kalbe E, et al. Education and occupation as proxies for reserve in aMCI converters and AD: FDG-PET evidence. *Neurology*. 2008;71:1342–1349.
23. Seidler A, Nienhaus A, Bernhardt T, et al. Psychosocial work factors and dementia. *Occup Environ Med*. 2004;61: 962–971.
24. Katzman R. Education and the prevalence of dementia and Alzheimer's disease. *Neurology*. 1993;43:13–20.
25. Wilson RS, Hebert LE, Scherr PA, et al. Educational attainment and cognitive decline in old age. *Neurology*. 2009;72: 460–465.

26. Bennett DA, Schneider JA, Tang Y, et al. The effect of social networks on the relation between Alzheimer's disease pathology and level of cognitive function in old people: a longitudinal cohort study. *Lancet Neurol*. 2006;5: 406–412.
27. Wilson RS, Arnold SE, Schneider JA, et al. Chronic distress, age-related neuropathology, and late-life dementia. *Psychosom Med*. 2007;69:47–53.
28. Royal Commission on Bilingualism and Biculturalism. *Report of the Royal Commission on Bilingualism and Biculturalism*. Ottawa: Queen's Printers; 1967.
29. Hakuta K, Bialystok E, Wiley E. Critical evidence: a test of the critical-period hypothesis for second-language acquisition. *Psychol Sci*. 2003;14:31–38.
30. Doraiswamy PM, Steffens DC, Pitchumoni S, et al. Early recognition of Alzheimer's disease: what is consensual? What is controversial? What is practical? *J Clin Psychiatry*. 1998;59:6–18.
31. CSHA. The incidence of dementia in Canada. The Canadian Study of Health and Aging Working Group. *Neurology*. 2000; 55:66–73.
32. CSHA. Canadian Study of Health and Aging: risk factors for Alzheimer's disease in Canada. *Neurology*. 1994;44:2073–2080.

