Early Life Instruction in Foreign Language and Music and Incidence of Mild Cognitive Impairment

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Abstract

Objective—To test the hypothesis that foreign language and music instruction in early life are associated with lower incidence of mild cognitive impairment (MCI) and slower rate of cognitive decline in old age.

Method—At enrollment in a longitudinal cohort study, 964 older persons without cognitive impairment estimated years of foreign language and music instruction by age 18. Annually thereafter they completed clinical evaluations that included cognitive testing and clinical classification of MCI.

Results—There were 264 persons with no foreign language instruction, 576 with 1–4 years, and 124 with >4 years; 346 persons with no music instruction, 360 with 1–4 years, and 258 with >4 years. During a mean of 5.8 years of observation, 396 participants (41.1%) developed MCI. In a proportional hazards model adjusted for age, sex, and education, higher levels (>4 years) of foreign language (hazard ratio [HR] = 0.687, 95% confidence interval [CI]: 0.482, 0.961) and music (HR = 0.708, 95% CI: 0.539, 0.930) instruction by the age of 18 were each associated with reduced risk of MCI. The association persisted after adjustment for other early life indicators of an enriched cognitive environment, and it was stronger for nonamnestic than amnestic MCI. Both foreign language and music instruction were associated with higher initial level of cognitive function, but neither instruction measure was associated with cognitive decline.

Conclusions—Higher levels of foreign language and music instruction during childhood and adolescence are associated in old age with lower risk of developing MCI but not with rate of cognitive decline.

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INTRODUCTION

Indicators of a cognitively enriched childhood environment, including household and community socioeconomic level (Kaplan et al., 2001; Singh-Manoux, Richards, & Marmot, 2005; Wilson, Scherr, Bienias, et al., 2005; Wilson, Scherr, Hoganson, et al., 2005; Fors, Lennartsson, & Lundberg, 2009) and frequency of cognitively stimulating activities (Everson-Rose, Mendes de Leon, Bienias, Wilson, & Evans, 2003; Fritsch et al., 2007; Wilson, Barnes, et al., 2005; Wilson, Scherr, Schneider, Tang, & Bennett, 2007; Wilson et al., 2013), have been associated with late-life cognitive functioning. However, there is limited knowledge about how differential childhood exposure to specific forms of cognitive enrichment is related to individual differences in cognitive aging and whether these associations are primarily with late life level of cognitive function (Everson-Rose et al., 2003; Wilson, Barnes, et al., 2005; Wilson, Scherr, Bienias, et al,. 2005; Wilson, Scherr, Hoganson, et al., 2005)or also with rate of cognitive decline (Wilson et al., 2007; Wilson et al., 2013). The present analyses focus on 2 learning experiences, foreign language instruction and music instruction, that are common but not universal during childhood, making for wide individual differences in exposure. In adulthood, bilingualism (Salvatierral & Rosselli 2010; Gold, Kim, Johnson, Kryscig, & Smith, 2013)and musical expertise (Hanna-Pladdy & MacKay, 2011; Hanna-Pladdy & Gajewski, 2012)are associated with higher level of cognitive function, suggesting that early life experience in these domains might be related to late life cognitive health, but few prior studies have investigated these issues(White-Schwoch, Carr, Anderson, Strait, & Kraus, 2013).

We used data from the Rush Memory and Aging Project to test the hypotheses that higher levels of foreign language and music instruction during childhood are associated in old age with lower risk of developing mild cognitive impairment (MCI) and slower rate of cognitive decline. Participants are 964 older persons without cognitive impairment at the time of enrollment. At baseline, participants indicated years of foreign language instruction and music lessons by age 18. Thereafter, they completed annual evaluations that included clinical classification of MCI and administration of a battery of cognitive function tests. In analyses, we tested for the hypothesized association of each form of instruction with incident MCI and trajectories of change in cognitive function.

METHODS

Participants

All participants are from the Rush Memory and Aging Project (Bennett, Schneider, Buchman, Mendes de Leon, & Wilson, 2005; Bennett et al., 2012), an ongoing longitudinal clinical-pathologic cohort study that began in 1997 and is continuing. Eligibility requires agreement to detailed annual clinical evaluations and brain autopsy at death. Older persons were recruited from retirement communities, social service agencies, subsidized housing facilities, and churches in the Chicago area. Following a presentation about the project, persons who expressed interest met with study personnel and written informed consent was obtained. The project was approved by the institutional review board of Rush University Medical Center.

At the time of these analyses, 1,543 individuals had completed the baseline evaluation and assessment of early life instruction. We excluded 458 persons found to have cognitive impairment at the baseline evaluation (64 with dementia and 394 with MCI). Of the remaining 1,085 individuals, 23 persons died before the first annual follow-up and 39 persons had been enrolled less than 1 year. Follow-up data were available on 964 of the 1,023 persons who were eligible for follow-up (94.2%) and analyses are based on this group. They had a mean age of 78.7 years at baseline (SD=7.4) and a mean of 14.6 years of education (SD=3.2); 740 (76.8%) were women.

Assessment of Early Life Instruction

As part of a structured interview at the baseline evaluation, participants were asked "By the age of 18, had you received any instruction in a foreign language ?"Those responding yes were asked "How many years?" All participants were also asked, "By the age of 18, had you taken any music lesions?" followed by "How many years?" for those responding yes.

Classification of Mild Cognitive Impairment

Each annual clinical evaluation included a structured medical history, neurological examination, and cognitive testing. On the basis of this evaluation, an experienced clinician diagnosed MCI in a 2-step process, as previously described in this (Boyle, Wilson, Aggarwal, Tang, & Bennett, 2006)and other (Bennett et al., 2002; Wilson, Aggarwal, et al., 2009) cohorts. First, an algorithm rated impairment in 5 cognitive domains (i.e., orientation, attention, memory, language, perception) based on educationally adjusted cutoff scores on 11 cognitive tests (Table 1; Bennett et al., 2002; Bennett et al., 2006). Second, after reviewing all cognitive data, education, occupation, and ratings of sensory problems, motor problems, and the participant's level of effort, a neuropsychologist agreed or disagreed with the algorithmic rating of each cognitive domain. In the event of disagreement, the neuropsychologist supplied a new impairment rating. The diagnosis of MCI required impairment in at least 1 of the 5 cognitive domains in the absence of dementia, defined following the criteria of the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association as a history of cognitive decline and impairment in at least 2 cognitive domains (McKhann et al., 1984). MCI was classified as amnestic if the memory domain was impaired and nonamnestic if memory was not impaired, as previously reported (Wilson, Schneider, et al., 2007; Wilson, Leurgans, Boyle, & Bennett, 2011). These MCI criteria have been related to intermediate levels of cognitive decline (Boyle et al., 2006; Bennett et al., 2002; Wilson et al., 2010)mortality (Bennett et al., 2002; Wilson, Aggarwal, et al., 2009), and Alzheimer's disease pathology (Bennett, Schneider, Wilson, Bienias, & Arnold, 2005) compared to dementia and no cognitive impairment.

Assessment of Cognitive Function

At each annual evaluation, a battery of 21 cognitive tests was administered in an approximately 45-minute session. The tests, listed in Table 1, included the Mini-Mental State Examination, a 30-item measure of global cognition (Folstein, Folstein, & McHugh, 1975); 8 items from Complex Ideational Material, a measure of auditory language comprehension (Goodglass & Kaplan, 1983); a 15-item version (Welsh et al., 1994) of the

Boston Naming Test (Kaplan, Goodglass & Weintraub, 1983); verbal fluency which involved naming examples of 2 semantic categories (animals, vegetables) in separate 1-minute trials (Welsh et al., 1994; Wilson et al; 2002); Digit Span Forward and Backward from the Wechsler Memory Scale-Revised (Wechsler, 1987); a modified form (Wilson et al., 2002) of Digit Odering (Cooper, Sagar, Jordan, Harvey, & Sullivan, 1991) in which strings of 2 to 9 digits were presented and the participant tried to say them back in ascending order; the oral form of the Symbol Digit Modalities Test involved rapidly identifying symbol digit matches in a 90-second trial (Smith, 1982); a modified version (Wilson et al; 2002) of Number Comparision (Ekstrom, French, Harman, & Kermen, 1976) that involved rapidly classifying pairs of 3-to 10 -digit strings as same or different in a 90-second trial; immediate and delayed story recall (Albert et al., 1991; Wilson et al., 2002) and Logical Memory Ia and IIa (Weschsler, 1987)which both involved recalling story details immediately and after a delay; 3 measures that required learning a list of 10 words (Welsh et al., 1994), with 3 trials of immediate recall (Word List Memory) and tests of delayed recall (Word List Recall) and recognition (Word List Recognition); a 15-item form (Wilson et al., 2002) of Judgment of Line Orientation (Benton, Sivan, Hamsher, Varney, & Spreen, 1994) that involved matching the angles subtended by lines; a 16-item form (Wilson et al., 2002) of Standard Progressive Matrices (Raven, Court, &Raven, 1972) which required identifying the missing section of a visual stimulus from 6 to 8 alternatives; a reading test, with 15 words selected from the National Adult Reading Test (Nelson, 1982) and later modifications (Blair & Spreen, 1989; Grober & Sliwinski, 1991); and a modified version (Wilson, Barnes, et al., 2005) of the Stroop Neurospychological Screening Test (Trenerry et al., 1989) which involved separate 30-second trials rapidly reading color names and naming colors.

The aims of cognitive testing were to support diagnostic decisions, as described in the previous section, and to characterize change in cognitive function over time. To reduce measurement error in longitudinal analyses, particularly floor and ceiling artifacts, we used composite outcomes based on 2 or more cognitive tests. The Mini-Mental State Examination and Complex Ideational Material were not included in these analyses because of their skewed distributions. All of the remaining 19 tests were used to form a composite measure of global cognition. Supported by factor analyses in this (Wilson, Barnes, & Bennett, 2003; Wilson, Barnes, et al., 2005)and other (Wilson et al., 2002; Wilson, Aggarwal, et al., 2009; Krueger, Wilson, Bennett, & Aggarwal, 2009) groups, composite measures of episodic memory, semantic memory, working memory, perceptual speed, and visuospatial ability were also formed (Table 1). In each case, raw test scores were converted to z scores using the baseline mean and SD in the entire cohort, and z scores of component tests were averaged to yield the composite score. Further information on the individual tests and derivation of the composite measures is published elsewhere (Wilson et al., 2002; Wilson, et al., 2003; Wilson, Barnes, et al., 2005).

Assessment of Other Covariates

Educational attainment was based on years of formal schooling. There were 3 indicators of early life socioeconomic status : mother's years of schooling, father's years of schooling, and the number of children in the family. Each indicator was converted to a z score, using the mean and SD of the entire cohort, and the z scores were averaged (with values for

number of children reversed to be consistent with the other indicators), as previously described (Wilson, Scherr, Hoganson, et al., 2005). At baseline, persons retrospectively rated cognitive resources and activities during childhood (Wilson, Barnes, et al., 2005). Specifically, a measure of the home cognitive environment was based on the number of 8 cognitive resources present in the home at age 12 (e.g., newspaper subscription, dictionary, encyclopedia, globe). They also rated frequency of participation in cognitively stimulating activities (e.g., reading a book, playing games like chess or checkers) from 1 (once a year or less) to 5 (every day or about every day). There were 11 items for ages 6 (3 items) and 12 (8 items) and 9 items for age 18. As in prior research (Wilson, Barnes, et al., 2005; Wilson et al, 2013), separate measures of childhood cognitive activity were formed by averaging the age 6–12 items and the age 18 items. Based on the medical history, we assessed 3 vascular risk factors: smoking (former or current), determined at baseline, and diabetes and hypertension, determined annually. The mean number present during the study period was used to quantify risk of vascular disease (Wilson, Arnold, Beck, Bienias, & Bennett, 2008; Wilson et al., 2012).

Statistical Analysis

All analyses were adjusted for age, sex, and education. We tested for the hypothesized association of early life instruction with incidence of MCI in a series of proportional hazards models. Because years of instruction was skewed (skewness of 2.8 for foreign language, 1.2 for music), we treated instruction as a categorical variable. To be consistent with prior research (White-Schwoch et al., 2013), we used 3 levels of instruction and contrasted a no instruction reference group with lower (1–4 years) and higher (>4 years) levels of instruction. We first modeled the 2 forms of instruction separately, then modeled them together, and then added covariates. We used a cause-specific relative hazard model (Lau, Cole, & Gange, 2009) to simultaneously estimate the association of instruction to amnestic and nonamnestic MCI. In a linear regression model, we regressed age at MCI diagnosis on the instruction measures. We used mixed-effects models to test for the association of the instruction measures with level of cognition at baseline and rate of cognitive change during follow-up. The initial outcome was the composite measure of global cognition. Subsequent models used composite measures of specific cognitive functions as outcomes.

RESULTS

There were 264 persons (27.4%) with no foreign language instruction by age 18, 576 (59.8%) with 1 to 4 years of instruction, and 124 (12.9%) with more than 4 years of instruction. There were 346 persons (35.9%) with no music instruction by age 18, 360 (37.3%) with 1 to 4 years, and 258 (26.8%) with more than 4 years. Higher level of foreign language instruction was associated with higher level of music instruction ($\chi^2[4] =68.8$, $p<0.001$). Higher level of foreign language ($F[2,961]=8.6$, $p<0.001$) but not music ($F[2,961]=1.2$, $p=0.308$) instruction was associated with older age at baseline. There were no gender differences in foreign language instruction ($\chi^2[2]=1.7$, $p=0.420$), but women reported more music instruction than men ($\chi^2[2]=7.6$, $p=0.023$). Higher levels of both instruction measures were associated with more years of education (foreign language $F[2,961]=71.4$, $p<0.001$; music $F[2,961]=63.0$, $p<0.001$), higher early life household

socioeconomic level (foreign language F[2,955]=47.5, p<0.001; music F[2,955]=67.9, p<0.001), more cognitive resources in the early home environment (foreign language F[2,958]=45.2, p<0.001; music F[2,958]= 67.9, p<0.001), and more frequent participation in cognitively stimulating activities at ages 6–12 (foreign language F[2,960]=23.8, p<0.001; music F[2,960]=25.6, p<0.001) and 18 (foreign language F[2,961]=83.3, p<0.001; music F[2,961]=77.1, p<0.001).

Early Life Instruction and Mild Cognitive Impairment

During a mean of 5.8 years (SD=3.5) of annual follow-up evaluations, 396 individuals (41.1%) developed MCI. As in previous research (Luck et al., 2010; Plassman et al., 2011; Roberts et al., 2012), MCI incidence rates increased with age, with a rate of 0.004 for ages less than 75 (33 cases in 833.03 person-years), 0.093 for ages 75–84 (179 cases in 1916.13 person-years), and 0.143 for ages 85 and older (184 cases in 1285.84 person years). These rates are higher than early estimates of the incidence of MCI (Larrieu et al., 2002; Busse, Bischkopf, Riedel-Heller, & Angermeyer, 2003; Solfrizzi et al., 2004) but are comparable to more recent population-based estimates (Manly et al., 2008; Luck et al., 2010; Plassman et al., 2011; Roberts et al., 2012). Some methodological features of the present study may contribute to high incidence rates including the high follow-up participation, relatively brief interval between follow-up observations, and high proportion of observations proximate to death. Compared to the 568 who remained cognitively intact, those who developed MCI were older (mean age of 80.8 vs 77.2, t[942.6]=7.8, p<0.001) and had a lower baseline level of cognition (mean Mini-Mental State Examination score of 28.2 vs 28.7, t[700.3]=5.0, p<0.001; mean global cognitive score of 0.124 vs 0.383, t[962]=9.6, p<0.001), but they had a similar percent of women (74.0 vs 78.7, χ^2[1]=2.9, p=0.089) and level of education (mean of 14.7 vs 14.5, t[962]=1.0, p=0.326).

We constructed a series of proportional hazards models to test for the hypothesized association of early life instruction with late-life risk of MCI. These and all subsequent analyses included terms to control for the potentially confounding effects of age (at baseline), sex, and years of formal education. In the first analysis (table 2, model A), both lower (1–4 years) and higher (>4 years) levels of foreign language instruction were associated with reduced risk of developing MCI relative to individuals with no foreign language instruction. In a subsequent analysis (table 2, model B), higher level of music instruction was associated with lower risk of MCI relative to those with no music instruction, with a nearly significant association for lower level of music instruction. With both forms of instruction in the same analysis (table 2, model C), higher levels of both forms of instruction were associated with lower risk of MCI with similar but not quite significant effects for lower levels of both forms of instruction.

Figure 1, which is based on model C, shows that higher levels (solid lines) of foreign language (upper panel) and music (middle panel) instruction were each associated with an approximately 30% lower risk of MCI compared to no instruction (dotted lines). The lower panel shows that these effects are additive, with risk of MCI approximately 60% lower with high levels of both forms of instruction (solid line; 4.6% of participants) compared with no foreign language or music instruction (dotted line; 15.0% of participants).

To determine whether cognitive activity or socioeconomic factors could account for the results, we repeated the previous analysis with 4 additional terms: frequency of cognitive activity at ages 6 and 12 (mean=3.02, SD=0.69), frequency of cognitive activity at age 18 (mean=3.07, SD=0.69), early life household socioeconomic status (mean=0.03, SD=0.74), and household cognitive resources at age 12 (mean=4.25, SD=2.03). As shown in table 1(model D), higher level of each form of early life instruction continued to be associated with lower risk of MCI.

Because vascular disease contributes to cognitive impairment in old age (Srikanth et al., 2003), we repeated model C with a term for the mean number of vascular risk factors during the study. Higher vascular risk was associated with higher risk of developing MCI (HR=1.389; 95% CI: 1.028, 1.878), but both foreign language instruction (HR for lower level = 0.775; 95% CI: 0.597, 1.008; HR for higher level = 0.641; 95% CI: 0.443, 0.926) and music instruction (HR for lower level = 0.791; 95% CI: 0.615, 1.016; HR for higher level = 0.674;95% CI: 0.504, 0.900) continued to be associated with lower risk of MCI. In a subsequent analysis, there was no evidence that the vascular risk index modified the association of early life instruction with late-life risk of MCI.

In studies of prevalent MCI, bilingualism has been associated with later retrospective estimate of age of onset (Ossher, Bialystok, Craik, Murphy, & Troyer, 2013; Bialystok, Craik, Binus, Ossher, & Freedman, 2013). Therefore, we regressed prospectively estimated age of MCI onset (n=396: mean=84.0, SD=6.5) on the early life instruction indicators. Foreign language instruction was associated with later age of onset (estimate for lower level = 0.790, SE=0.309, p=0.011; estimate for higher level = 1.071, SE=0.434, p=0.014) but music instruction was not (estimate for lower level = 0.574, SE=0.297, p=0.054; estimate for higher level = 0.490, SE=0.340, p=0.150).

MCI was amnestic in 219 (55.3%) and nonamnestic in 177 (44.7%). Compared to those who developed amnestic MCI, people who developed nonamnestic MCI were younger at baseline (mean of 79.5 vs 81.8, t[344.4]=3.6, p<0.001) and more likely to be female (80.2 vs 69.0, χ^2 [1]=6.5, p=0.011) but had similar levels of education (mean of 15 vs 14.5, t[394]=1.5, p=0.134) and global cognition at baseline (mean Mini-Mental State Examination score of 28.3 vs 28.1, t[394]=1.0, p=0.299; mean global cognitive score of 0.161 vs 0.094, t[394]=1.6, p=0.109). To see if early life instruction was differentially related to MCI subtypes, we constructed a cause-specific relative hazard model which made it possible to include both MCI subtypes in a single model (Table 3). Both forms of early life instruction were associated with lower incidence of nonamnestic MCI (right side of Figure 2), but neither was associated with incidence of amnestic MCI (left side of Figure 2).

Early Life Instruction and Cognitive Aging

We analyzed change in cognitive function during the observation period in a mixed-effects model to determine whether early life instruction was related to risk of MCI because of an association with level of cognitive function, rate of cognitive decline, or both. In this analysis, lower (estimate=0.191, SE=0.031, p<0.001) and higher (estimate=0.260, SE=0.045, p<0.001) levels of foreign language instruction and lower (estimate=0.092, SE=0.031, p=0.003)and higher (estimate=0.133, SE=0.035, p<0.001)levels of music

instruction were each associated with higher level of global cognitive function at baseline (mean=0.277, SD=0.434). However, neither foreign language instruction (estimate for lower level = 0.009, SE=0.008, p=0.291; estimate for higher level = −0.011, SE=0.012, p=0.354) nor music instruction (estimate for lower level =0.000, SE=0.008, p=0.992; estimate for higher level =0.003, SE=0.00 9, p=0.719) was related to rate of global cognitive decline. Figure 3, which is based on this analysis, shows a dose response type relationship between early life level of instruction and late life level of global cognition for foreign language instruction (upper panel), music instruction (middle panel), and the 2 forms of instruction combined (lower panel).

To determine whether the association of early life instruction with late life cognition varied across cognitive domains, we repeated the previous analysis with composite measures of specific cognitive functions (Table 4). Both foreign language instruction and music instruction were associated with higher level of baseline function in all cognitive domains. However, with the exception of a marginal association of lower (but not higher) level of foreign language instruction with rate of decline in perceptual speed, the early life instruction measures were not associated with rate of cognitive decline.

DISCUSSION

In a group of nearly 1,000 older persons without evidence of cognitive impairment at study onset, more than 40% developed MCI during a mean of 5.8 years of follow-up observation. Foreign language and music instruction during youth (i.e., at least 5 years of instruction by age 18) were each associated with lower risk of developing MCI due to the association of instruction with higher initial level of cognitive function rather than with rate of cognitive decline. The results suggest that cognitively enriching experiences during childhood are related to cognitive health in old age.

Although there has been little prior research on the long term consequences of early life instruction (White-Schwoch et al., 2013), the results are broadly consistent with prior research showing experience dependent neuroplastic changes in animals (Marham & Greenough, 2004; Barnes & Finnerty, 2010; Qui, Huang, Lu, et al., 2012) and humans (Draganski, Gaser, Kempermann, et al, 2006; Schmidt-Wilcke, Rosengarth, Luerding, Bogdahn, & Greenlee, 2010; Woollett & Maguire, 2011) following exposure to novel environmental contingencies. The observed association of early life instruction in a foreign language or music with higher level of cognition in old age is consistent with previous cross-sectional research showing that adults with expertise in a foreign language (Salvatierra & Rosselli, 2010; Gold et al., 2013) or music (Hanna-Pladdy & Mackay, 2011; Hanna-Pladdy & Gajewski, 2012)perform better on cognitive tests than adults without such expertise. We found no association between early life training and late-life rate of cognitive decline. This is consistent with a previous study that found no association between bilingualism and cognitive decline in old age(Zahodne, Schofield, Farrell, Stern, & Manly, 2013) and a much broader literature showing that another measure of early life instruction, years of formal education, is related to level of cognition in old age but not to rate of decline (Van Dijk, Van Gerven, Van Boxtel, Van der Elst, & Jolles, 2008; Karlamangla et al., 2009; Wilson, Hebert, et al., 2009).

In persons with prevalent MCI, bilingualism has been associated with later age of symptom onset (Ossher, Bialystok, Craik, Murphy, & Troyer, 2013; Bialystok, Craik, Binus, Ossher, & Freedman, 2013), but the insidious onset of MCI makes it difficult to estimate, particularly retrospectively. The present results add to current knowledge by linking early life instruction to risk of MCI in a prospective study, by showing the association for 2 different forms of early life instruction, and by showing that early life instruction predicts incident MCI by virtue of an association with level of cognition rather than with rate of cognitive decline. An unexpected observation was that early life instruction was related to risk of nonamnestic MCI but not amnestic MCI. The significance of this finding is uncertain, however, since early life instruction was related to level of function in all cognitive domains, including episodic memory (Table 4).

These findings are consistent with the cognitive reserve hypothesis (Barulli & Stern, 2013) and research in life course epidemiology (Whalley, Dick, & McNeill, 2006) linking early life exposures to brain and cognitive development leading to higher peak performance during adulthood and thereby providing additional cognitive reserve that can delay the onset of MCI despite a lack of association with cognitive decline. That is, compared to people with less exposure to early life instruction those with more exposure begin late life with a higher level of cognitive ability, and because they decline at the same rate as individuals with less instruction exposure, it takes longer for their cognitive ability to slip to a level low enough to trigger a diagnosis of MCI. Thus, the observed association between early life instruction and late-life level of cognitive function was probably also present in early life given the strong correlation between early life cognitive ability and late-life cognitive ability (Gow et al, 2011; Deary, Pattie, & Starr, 2013). In prior research, music lessons (Schellenberg, 2004; Moreno et al., 2011) and school attendance (Ceci & Williams, 1997) have been associated with enhanced cognitive skills in children, suggesting that the instruction-cognition correlation in the present study is partly due to additional structured learning experience stimulating cognitive growth and development during childhood. In the present study, however, at least 5 years of foreign language instruction was associated with an additional 0.260-unit on the baseline global cognitive score, which is nearly 60% of the standard deviation at baseline (0.434), and the baseline global cognitive score of an individual with high levels of both forms of instruction was 0.393-unit higher than the score of an individual with no instruction in either area, a difference which is more than 90% of the baseline standard deviation. The substantial size of these effects suggests that other factors are probably involved. In particular, it is likely that the instruction-cognition association is reciprocal so that children with higher levels of cognitive ability likely gravitate toward more challenging academic pursuits and these additional structured learning experiences likely stimulate subsequent cognitive growth and development (Corrigall, Schellenberg, & Misura, 2013).

The strengths and limitations of these findings should be noted. The availability of a mean of 5.8 years of annual follow-up with a high rate of follow-participation in a relatively large cohort enhanced our ability to estimate the association of the instruction measures with cognitive outcomes. That results were comparable with different types of instruction suggests that they are reliable. Classification of MCI was based on a comprehensive neuropsychological assessment, as currently recommended (Bondi & Smith, 2014). Because

the diagnosis of MCI was made by persons blinded to previously collected data, incidence of MCI and change in cognitive function are independent outcomes, and the 2 outcomes allowed us to show that the association of early life instruction with late-life cognitive health is clinically significant but does not involve cognitive decline. The main limitation is that we did not assess foreign language or musical experiences during the approximately 60 year period from age 18 to enrollment in the current study (mean age at baseline = 78.7). It is likely that some portion of the association of early life instruction with late-life cognition is mediated by the extent to which these skills were exercised during the adulthood. In addition, participants were selected and so the generalizability of the results remains to be determined, and information about early life instruction was obtained by retrospective report which may have biased results.

Acknowledgments

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Figure 1.
Relation of early life years of foreign language instruction (upper panel in red), music instruction (middle panel in blue), and the 2 forms of instruction combined (lower panel in green) to cumulative hazard of developing mild cognitive impairment in late-life, from a proportional hazards model adjusted for age, sex, and education.

Figure 2.
Relation of early life years of foreign language instruction (upper panels in red), music instruction (middle panels in blue), and the 2 forms of instruction combined (lower panels in green) to cumulative hazard of developing amnestic (left side) and nonamnestic (right side) mild cognitive impairment in late-life, from a cause-specific relative hazard model adjusted for age, sex, and education.
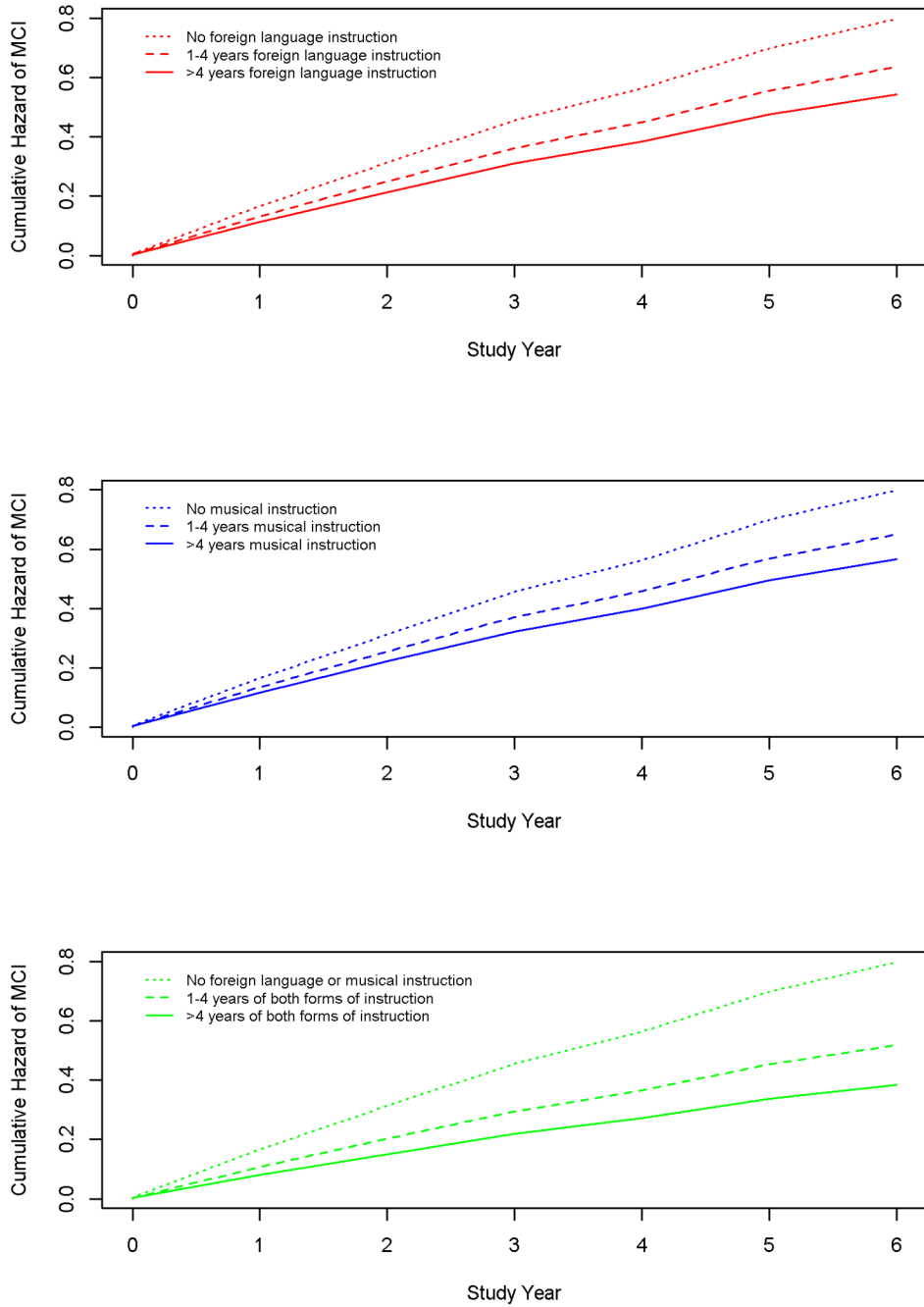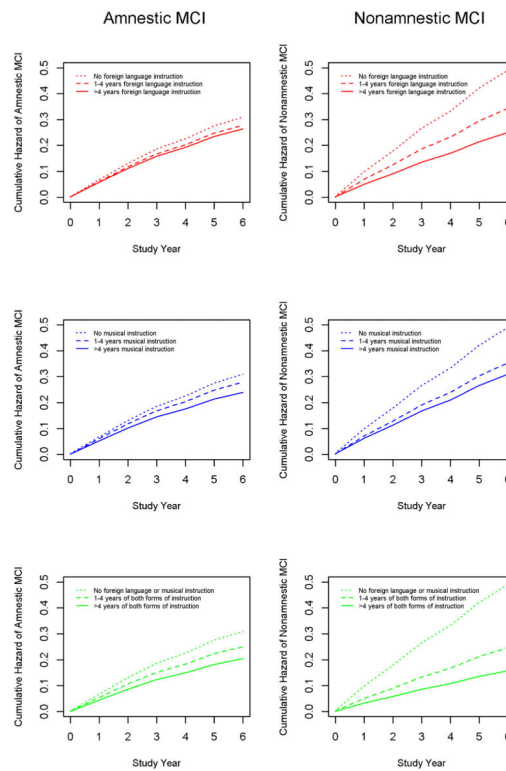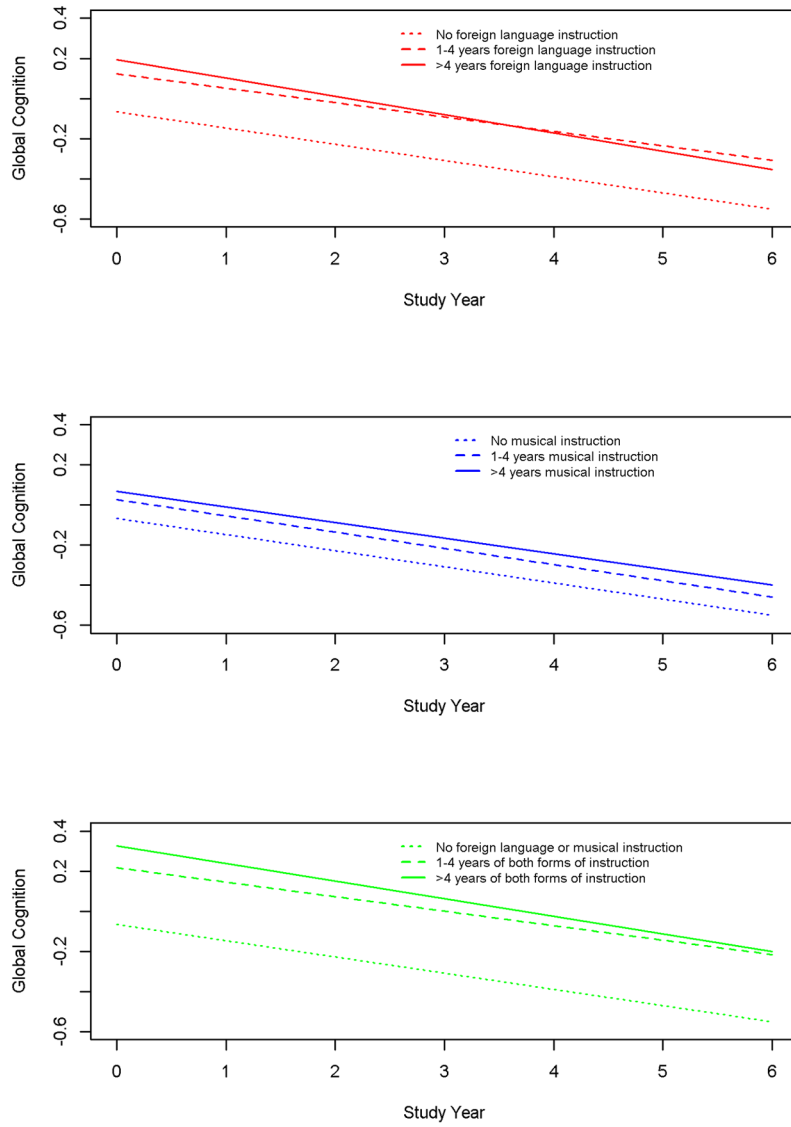
Figure 3.
Relation of early life years of foreign language instruction (upper panel in red), music instruction (middle panel in blue), and the 2 forms of instruction combined (lower panel in green)to level of and change in global cognition in late life, from a mixed-effects model adjusted for age, sex, and education.

Table 1

Role of tests in determining cognitive impairment for clinical classification and assessing cognitive change over time

Test (maximum score)	Impairment Cutoffs by Education				Hypothesized Cognitive Domains	
	<8	8–11	12–16	>16	Clinical Classification	Longitudinal Analyses
MMSE orientation (10)	<7	<8	<8	<9	Orientation	
Complex Ideational Material (8)	<7	<7	<7	<7	Language	
Boston Naming Test (15)	<9	<10	<11	<13	Language	Semantic memory
Verbal Fluency (75)	<9	<10	<10	<12	Language	Semantic memory
Digital Span Backward (12)	<3	<4	<5	<5	Attention	Working memory
Symbol Digit Modalities Test (110)	<8	<16	<21	<25	Attention	Perceptual speed
Logical Memory IIa (25)	<3	<4	<5	<9	Memory	Episodic memory
Word List Recall (10)	<3	<5	<5	<5	Memory	Episodic memory
Word List Recognition (10)	<8	<9	<9	<9	Memory	Episodic memory
Judgment of Line Orientation (15)	<3	<5	<7	<8	Perception	Visuospatial ability
Standard Progressive Matrices (16)	<5	<6	<7	<8	Perception	Visuospatial ability
Reading Test (15)						Semantic memory
Digit Span Forward (12)						Working memory
Digit Ordering (16)						Working memory
Number Comparison (48)						Perceptual speed
Stroop reading (80)						Perceptual speed
Stroop naming (80)						Perceptual speed
Logical Memory Ia (25)						Episodic memory
Word List Memory (30)						Episodic memory
Immediate story recall (12)						Episodic memory
Delayed story recall (12)						Episodic memory

Note. MMSE, Mini-Mental State Examination.

Table 2

Relation of early life instruction to late-life risk of incident mild cognitive impairment

Instruction Years by Age 18	Model A		Model B		Model C		Model D	
	HR	95% CI	HR	95% CI	HR	95%, CI	HR	95% CI
Foreign language								
None (reference group)								
1–4 years	0.740	0.570, 0.960	0.783	0.609, 1.005	0.796	0.624, 1.017	0.802	0.621, 1.035
>4 years	0.616	0.428, 0.888	0.650	0.488, 0.866	0.681	0.482, 0.961	0.692	0.485, 0.987
Music								
None (reference group)								
1–4 years			0.815	0.644, 1.030	0.818	0.641, 1.044		
>4 years			0.708	0.539, 0.930	0.716	0.538, 0.953		

Note. From 4 separate proportional hazards models adjusted for age, sex, and education. Model D also adjusted for early life indicators of cognitive activity frequency and household socioeconomic status. HR, hazard ration; CI, confidence interval.

Table 3

Relation of early life instruction to subtypes of incident MCI

Instruction Years by Age 18	Amnestic MCI (n=219)		Nonamnestic MCI (n=177)	
	HR	95% CI	HR	95% CI
Foreign language				
None (reference group)				
1–4 years	0.888	0.626, 1.261	0.683	0.474, 0.986
>4 years	0.841	0.527, 1.341	0.491	0.281, 0.857
Music				
None (reference group)				
1–4 years	0.893	0.643, 1.240	0.705	0.490, 1.014
>4 years	0.760	0.519, 1.114	0.617	0.406, 0.937

Note. From a cause-specific relative hazard model adjusted for age, sex, and education. MCI, mild cognitive impairment; HR, hazard ratio; CI, confidence interval.

Table 4

Relation of early life instruction to late-life cognitive level and rate of change

Model Term	Episodic Memory			Semantic Memory			Working Memory			Perceptual Speed			Visuospatial Ability		
	Estimate	SE	p	Estimate	SE	p	Estimate	SE	p	Estimate	SE	p	Estimate	SE	p
Time	−0.078	0.010	<0.001	−0.069	0.009	<0.001	−0.078	0.008	<0.001	−0.116	0.009	<0.001	−0.056	0.008	<0.001
Language 1–4 years	0.187	0.041	<0.001	0.203	0.038	<0.001	0.161	0.044	<0.001	0.217	0.047	<0.001	0.112	0.043	0.009
Language > 4 years	0.271	0.059	<0.001	0.219	0.055	<0.001	0.185	0.064	0.004	0.259	0.068	<0.001	0.165	0.063	0.009
Music 1–4 years	0.066	0.040	0.100	0.116	0.037	0.002	0.070	0.044	0.107	0.072	0.046	0.118	0.211	0.042	<0.001
Music > 4 years	0.104	0.046	0.024	0.148	0.042	<0.001	0.119	0.050	0.018	0.131	0.053	0.013	0.234	0.049	<0.001
Language 1–4 years × time	0.015	0.010	0.112	0.004	0.009	0.656	0.010	0.008	0.204	0.004	0.009	0.627	0.023	0.009	0.008
Language > 4 years × time	−0.003	0.014	0.828	0.003	0.013	0.794	−0.002	0.012	0.898	0.005	0.013	0.675	0.014	0.012	0.247
Music 1–4 years × time	0.005	0.009	0.623	−0.010	0.009	0.268	0.006	0.008	0.428	0.006	0.009	0.500	−0.006	0.008	0.488
Music > 4 years × time	0.006	0.011	0.555	−0.002	0.010	0.864	0.013	0.009	0.139	0.003	0.010	0.790	−0.005	0.009	0.596

Note. From 5 separate mixed-effects models adjusted for age, sex, and education. SE, standard error.