Cohort Effects in Age-Associated Cognitive Trajectories

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ABSTRACT (150 words)

The age-specific prevalence and incidence of dementia and cognitive impairment in the United States have been either stable or even slightly declining during the 1980s-1990s. One of the suggested but as yet untested reasons of for this improving cognitive function over time is higher educational attainments among more recent cohorts. We used data from two large prospective population-based epidemiological dementia studies, covering the period of 1902 to 2012. Our aims are to examine whether 1) cohort effects exist in age-associated trajectories of cognitive functions, and 2) the observed cohort effects could be explained by educational attainment. We examined age*cohort interactions in mixed effects models with/without controlling for education effects. We observed strong cohort effects with the more recent cohorts showing less age-associated cognitive declines. Surprisingly the cohort effects remained very significant after controlling for educational effects. Factors other than education are likely responsible for the cohort effects in cognitive decline.

INTRODUCTION

It has been reported that the age-specific prevalence and incidence of dementia and cognitive impairment in the United States have been either stable or even declining during the 1980s-1990s. (Rocca *et al.*, 2011) (Langa *et al.*, 2008) A recent Dutch study also showed age-adjusted dementia incidence rates to be consistently, although non-significantly, lower in the sub-cohort assessed in 2000 than that assessed a decade earlier.(Schrijvers *et al.*, 2012) In behavioral sciences, one of the persistent predictors of disease prevalence, incidence and mortality is years of educational attainment. Although there is still a debate regarding the mechanism underlying the association between education and overall health (e.g., income, accessibility to health care, life style and environment, mother's nutrition during prenatal period, nutrition during infancy, etc), we expect that cognitive functions can be very much affected by educational attainment. This is because in addition to the potential reasons of educational effects on overall health suggested above, test-taking skill (which could affect performance on neuropsychological tests used to measure cognitive functions) can be also associated with educational attainment. Yet, there is a paucity of studies which examine how much educational attainment explains the cohort effects in cognitive aging, specifically longitudinal age associated cognitive declines. In this study, we assessed whether 1) cohort effects exist in age associated trajectories of cognitive functions, and 2) the observed cohort effects would be explained by changes in educational attainment among cohorts. Trajectories of neuropsychological tests which tap 3 domains (psychomotor speed, executive function and language) were examined and compared among cohorts born between 1902 and1911, 1912 and 1921, 1922 and 1931, and 1932 and1943.

Data:

Data comes from two large epidemiological study of dementia: the Monongahela Valley Independent Elders Study (aka, MoVIES) and the Mon-Yough Healthy Aging Team study (aka, MYHAT). Both studies recruited

age-stratified random samples of individuals aged 65+ years from the Voter Registration lists for targeted communities in southwestern Pennsylvania. Brief descriptions of each study follow.

MoVIES . This project recruited and assessed 1681 individuals during 1987-1989 from a group of largely rural communities, with the goal of following them biennially over time to investigate incidence, and risk factors for cognitive impairment and dementia. The detail description of recruitment and follow-up protocol is found elsewhere.(Ganguli *et al.*, 1993; Ganguli *et al.*, 2000) At baseline, the study response rate was approximately 60%, with 2% of non-mortality drop out between subsequent biennial assessments. Data collection was completed in 2001.

MYHAT. This project recruited and assessed 1982 individuals during 2005-2007 from a group of small-town communities, with the objective of following them annually over time to investigate outcomes, and predictors of outcomes in mild cognitive impairment. The detail description of recruitment and follow-up protocol is found elsewhere.(Ganguli *et al.*, 2010; Ganguli *et al.*, in press) The study is currently in the 5th wave of data collection. At baseline, the study response rate was approximately 63%. (Ganguli *et al.*, 2009)

We combined the data from the two studies and categorized subjects into the following 4 birth cohorts: those born between 1902 and 1911, between 1912 and 1921, between 1922 and 1931, and between 1932 and 1943. We excluded 50 subjects born before 1901 due to small sample size .

Educational attainment: We used 3 education categories: less than high school education, completed high school education but less than college education, and completed college or more education.

Neuropsychological tests: The following four neuropsychological tests (domain) were administered in the exact same way across two studies and used in this study: trail making test A (psychomotor speed)(Reitan and Wolfson, 1985), trail making test B (executive function)(Reitan and Wolfson, 1985) and verbal fluency letters (executive function, hence forth noted as letter fluency) and verbal fluency category animals (language, hence forth category fluency).(Lezak, 1995) The time taken to complete the test is conventionally used for scoring trails A and B. However, to address skewed distribution and ceiling effects (e.g., time of completion is

truncated after the maximum duration allowed), we calculated correct connections/second in this analysis. Although both studies included several memory tests, they used different tests as MoVIES was focused on dementia and MYHAT was focused on mild cognitive impairment; hence we have not examined memory tests in these analyses. For fair comparisons of magnitudes of coefficients across 4 cognitive tests, all tests are standardized using mean and standard deviation of each test score at baseline.

Statistical analysis:

Differences by birth-cohorts in educational attainment were compared within each age category (65-74, 75-84, 85 and older) using Pearson chi-square statistics. We used mixed effects models with the outcomes being scores on each cognitive test. We ran three models for each outcome. In Model 1, we examined age effect on cognitive functions, controlling for sex. In Model 2, we added cohort and cohort * age interactions (for assessing cohort effect on age-associated cognitive trajectories), controlling for sex. In Model 3, we further added education, age*education and age*education*cohort interactions. Intercept and age were treated as random effects. Model fitness was examined through visual inspection of residuals and formal statistical tests.

Results

Table 1 shows that average education level increased with successive birth cohorts. 60.0%, 61.5%, 36.7%, and 14.8% of the individuals born in 1882-1901, 1902-1911, 1912-1921, and 1922-1931 had less than high school graduate level education, respectively, while only 6.6% of the individuals born in 1932-1943 had less than high school graduate level education. Table 2 shows results of mixed effects models. For all 4 outcomes (cognitive test scores) we observed significant baseline birth-cohort effects as well as significant age* birth-cohort interaction effects in Model 1, using the most recent birth-cohort as the reference group. A negative coefficient means that the earlier birth cohort has steeper age-associated cognitive declines. The largest age-associated decline was observed for psychomotor speed and executive functions; coefficients for age were -0.06, -0.06, -0.02, -0.05 for speed, executive, letter fluency, and category fluency, respectively. In Model 2, indicators of

birth cohorts were included. Cohort differences in baseline scores were found for all cohorts (1902-1911, 1912-1921, and 1922-1931 cohorts) in comparison with the most recent cohort (1931-1941) with executive functions measured by trail making test B being the largest in magnitude. As for age-associated trajectory, difference was seen between the most recent cohort and the cohort born earliest (1902-1911) in psychomotor speed and language (category fluency). For executive functions, significant differences in trajectories were seen between the most recent cohort and two earlier cohorts (1902-1911, 1912-1921) in letter fluency, and between the most recent cohort and all of the previous cohorts in trail making B with coefficients being -0.07, -0.05, and -0.03 for cohort 1902-1911, 1912-1921, and 1922-1931, respectively. These patterns observed in cognitive test scores and cohorts remained after we included education, age*education and age*education*cohort effects in Model 3. As no 3-way interactions was significant, none were included in the final model reported.

Discussion

Using two large epidemiological dementia cohort studies conducted in the same region, we assessed birth cohort effects in age-associated trajectory of cognitive functions. We examined 3 domains of cognitive functions including psychomotor speed, executive functions, and language. Four birth cohorts—those born between 1902 and 1911, 1912 and 1921, 1922 and 1931 and 1932-1941 (the reference group) — were compared in their baseline cognitive test scores and also their subsequent trajectories. Cohort effects were observed in all cognitive domains, with consistent differences shown between the earliest born cohort and the most recent cohort across all cognitive domains and executive functions having the strongest and persistent differences between the most recent and other three cohorts. Education did not attenuate any of these associations.

In the social science field, socio economic status (SES), for which educational attainment is the major component, has been one of the robust predictors of mortality and health. One of the earliest and most comprehensive studies on the SES and mortality in the United States was conducted by Kitagawa and Hauser, a few decades ago. (Kitagawa and Hauser, 1973). They found a strong inverse relation between mortality and educational attainment, with the range of mortality differentials being larger among individuals 25-64 years of

age than among older individuals, and greater among women than men. The mortality disadvantage of those with lower socio economic status (SES) has been found to be mainly due to their unhealthy behaviors including smoking, alcohol consumption, dietary patterns, and physical activity. (Laaksonen *et al.*, 2008; Lynch *et al.*, 1997; Martikainen *et al.*, 2003) (Lantz *et al.*, 1998; Makinen *et al.*, 2012; Schrijvers *et al.*, 1999; Strand and Tverdal, 2004; van Oort *et al.*, 2005; Woodward *et al.*, 2003) For example, using nationwide Finnish health behavior surveys from the years 1979 to 2001, Laaksonen et. al. (Laaksonen *et al.*, 2008) found that educational level showed a graded association with cardiovascular disease, coronary heart disease, stroke and all-cause mortality. They found smoking, low vegetable consumption, and physical inactivity explained a substantial part of educational level differences in the mortality. Recent studies conducted in England using a very large cohort of civil servants also showed the strong association between socioeconomic position and mortality.(Stringhini et al., 2010; Stringhini et al., 2012) They showed that the association was substantially accounted for by adjustment for health behaviors including diet, physical activities, and alcohol consumption.(Stringhini *et al.*, 2010), and almost half of the differences in incidence of type 2 diabetes by SES status (Stringhini *et al.*, 2012) was explained by potentially modifiable risk factors such as health behaviors and obesity.

As for cognitive health and educational attainment, it has been observed that during the 20th century, subsequent cohorts always outperformed previous generations on IQ tests. This is known as the Flynn Effect. (Flynn, 1987) Schaie et. al. (2005), using the Seattle Longitudinal Study, further showed that cohort differences in intelligence occurred even before 1900s (earlier than shown in Flynn's studies), with a more dramatic improvement being observed between those born before 1900 (median birth year of 1896) and those born in the early 1900s (median birth year 1924), and somewhat diminished improvements among subsequent cohorts. Schaie et. al.(2005) speculated that a dramatic increase in educational attainment among those born around 1924 (mainly due to the GI Bill), compared with those born around 1896, could have contributed to marked cohort differences for both verbal ability (so-called crystallized intelligence which is thought to be improved through schooling) and inductive reasoning (fluid intelligence). Based on past studies on links between overall health and SES/education, and between educational attainment and cognition, we hypothesized that we would see cohort effects in age associated trajectory of cognitive functions in both language fluency and

executive function, and that the cohort differences in trajectory be attenuated if we control for educational attainment in the model. Consistently with Flynn's study results, we found strong cohort effects in executive functions (fluid ability). However, we also found cohort effects in verbal ability at least between the earliest born cohort (1902-1911) and the most recent cohorts (1932-1943). Unexpectedly, educational attainment did not attenuate any of the cohort differences either in baseline test scores or ins age-associated trajectories of cognitive scores. Potential explanations for the latter finding include: 1) educational attainment is not a good indicator of its downstream effects including life style factors and comorbidity associated with cognitive well-being in our study region, 2) as Kitagawa and Hauser (Kitagawa and Hauser, 1973) has shown, education effect is stronger for those in younger and middle aged; once subjects reach 65 or older age (the age group examined in this analysis), education effects might diminish. Possibly other factors than educational attainment (e.g., general improvement in nutritional intake, genetic factors) could play larger roles in determining cognitive trajectory. Selective drop out and mortality could also distort the true association. However, the bias mostly occurs when follow-up is truncated (due to drop out) and therefore further cognitive declines cannot be observed. If this is the case, earlier cohorts with higher mortality should show better cognitive trajectory given other things equal (i.e., trajectory is truncated before declining). This was not the case in our finding.

Cohort effects in age-associated trajectory of cognitive function could have a large impact on the incidence and prevalence of late-onset dementia. Although examining this impact is beyond the scope of our current study, there have been some indications (without statistical significance) that age-specific dementia prevalence has been either stable or declined slightly between 1980s and 1990s in the US. (Rocca *et al.*, 2011) (Langa *et al.*, 2008) Incidence also showed statistically non-significant yet declining trends in Europe; Sacuiu et. al. (Sacuiu *et al.*, 2010) showed dementia incidence between age 70 and 75 years was 5.0% in cohort born in 1901-1902 and 4.4% in cohort born in 1930 during the 5 years of follow-up in Sweden. Schrijvers et. al. (Schrijvers *et al.*, 2012) also showed that dementia incidence has decreased between 1990 and 2005 using data from the Rotterdam Study. The latter study further showed that participants in 2005-2006 had statistically significant larger total brain volumes and less cerebral small vessel disease (although non-significant in men) than participants in 1995-1996. In contrast to the US and some European countries, however, all-cause

dementia prevalence seems to be increasing in some other regions including Japan, possibly due to increase in metabolic diseases. (Dodge *et al.*, 2012) The large increase in obesity and metabolic diseases in the US and other regions in the 21st century (Olshansky *et al.*, 2005) could also change the future trend in dementia incidence and prevalence. Therefore, it is still very much uncertain whether the compression of morbidity (Fries, 1980) could apply to the cognitive health even if we find the upward cohort effects in cognitive test scores and the resultant increase in cognitive reserve. The strength of our study include that the neuropsychological batteries were administered in the same manner between the two cohorts, both studies were conducted in the same region with relatively large sample size with low levels of in- and out-migrations.

Conclusions

We observed strong cohort effects with the more recent cohorts showing less age-associated cognitive declines. Surprisingly the cohort effects remained very significant after controlling for educational effects. Factors other than education are likely responsible for the cohort effects in cognitive decline among those aged 65 and older.

Acknowledgements:

Funding sources: R01AG033581, R01AG07562, P30AG008017, R01AG033581.

Table 1: Combined MoVIES-MYHAT sample: **Educational Level by Birth Cohort**				
Birth Cohort	**Education**			
	<High School Graduate	**High School Graduate**	**>High School Graduate**	**Total**
	n (row%)	n (row%)	n (row%)	
1.1882-1901	30 (60.00%)	8 (16.00%)	12 (24.00%)	50
2.1902-1911	259 (61.52%)	64 (15.20%)	98 (23.28%)	421
3.1912-1921	514 (36.74%)	547 (39.10%)	338 (24.16%)	1399
4.1922-1931	159 (14.79%)	506 (47.07%)	410 (38.14%)	1075
5.1932-1943	47 (6.55%)	307 (42.76%)	364 (50.70%)	718

Birth cohort 1882-1901 was not used in the subsequent analysis due to small sample size.

Table 2. Results of mixed effects model: birth-cohort effects on age associated cognitive trajectories before and after controlling for education effects

2A. Psychomotor Speed (Trail Making A, connections/second)

	Model 1			Model 2			Model 3		
	Coeff.	**SE**	**P-Value**	**Coeff.**	**SE**	**P-Value**	**Coeff.**	**SE**	**P-Value**
Intercept	-0.38	0.02	<.0001	0.07	0.07	0.32	0.16	0.07	0.03
Female	0.20	0.03	<.0001	0.20	0.03	<.0001	0.19	0.03	<.0001
Age80	-0.06	0.002	<.0001	-0.04	0.01	<.0001	-0.04	0.01	<.0001
Cohort 1902 to 1911				-0.84	0.08	<.0001	-0.62	0.08	<.0001
Cohort 1912 to 1921				-0.57	0.07	<.0001	-0.44	0.07	<.0001
Cohort 1922 to 1931				-0.29	0.08	0.00	-0.26	0.07	0.00
Age80*Cohort 1902 to 1911				-0.03	0.01	0.00	-0.05	0.01	0.00
Age80*Cohort 1912 to 1921				-0.01	0.01	0.41	-0.01	0.01	0.24
Age80*Cohort 1922 to 1931				-0.001	0.01	0.91	-0.01	0.01	0.38
Education <HS							-0.46	0.04	<0.001
Education =HS							-0.08	0.03	0.01
Age80*Education <HS							0.004	0.004	0.27
Age80*Education =HS							0.000	0.004	0.98

Notes:
Reference groups: Male; Cohort 1932 to 1943; Age80*Cohort 1932 to 1943; age80*Education >HS.
Age variable was centered at age 80 (i.e., age at each assessment – 80).
Age and intercept are treated as random effects.

2B. Executive Functions (Trail Making B, connections/second)

	Model 1			Model 2			Model 3		
	Coeff.	**SE**	**P-Value**	**Coeff.**	**SE**	**P-Value**	**Coeff.**	**SE**	**P-Value**
Intercept	-0.38	0.02	<.0001	0.48	0.08	<.0001	0.59	0.08	<.0001
Female	0.14	0.03	<.0001	0.14	0.03	<.0001	0.12	0.03	<.0001
Age80	-0.06	0.002	<.0001	-0.01	0.01	0.33	-0.005	0.01	0.24
Cohort 1902 to 1911				-1.37	0.09	<.0001	-1.08	0.08	<.0001
Cohort 1912 to 1921				-1.02	0.08	<.0001	-0.85	0.08	<.0001
Cohort 1922 to 1931				-0.61	0.08	<.0001	-0.56	0.08	<.0001
Age80*Cohort 1902 to 1911				-0.07	0.01	<.0001	-0.08	0.01	<.0001
Age80*Cohort 1912 to 1921				-0.05	0.01	<.0001	-0.05	0.01	<.0001
Age80*Cohort 1922 to 1931				-0.03	0.01	<.0001	-0.04	0.01	0.00
Education <HS							-0.61	0.04	<.0001
Education =HS							-0.12	0.03	0.00
Age80* Education <HS							0.007	0.004	0.05
Age80* Education =HS							0.004	0.004	0.90

Notes:
Reference groups: Male; Cohort 1932 to 1943; Age80*Cohort 1932 to 1943; age80*Education >HS.
Age variable was centered at age 80 (i.e., age at each assessment – 80).
Age and intercept are treated as random effects.

2C. Executive Functions (Letter Fluency P and S)

	Model 1			Model 2			Model 3		
	Coeff.	**SE**	**P-Value**	**Coeff.**	**SE**	**P-Value**	**Coeff.**	**SE**	**P-Value**
Intercept	-0.18	0.03	<.0001	0.39	0.08	<.0001	0.52	0.08	<.0001
Female	0.17	0.03	<.0001	0.17	0.03	<.0001	0.17	0.03	<.0001
Age80	-0.02	0.002	<.0001	0.004	0.01	0.53	0.006	0.007	0.45
Cohort 1902 to 1911				-0.91	0.09	<.0001	-0.63	0.09	<.0001
Cohort 1912 to 1921				-0.68	0.08	<.0001	-0.50	0.08	<.0001
Cohort 1922 to 1931				-0.45	0.08	<.0001	-0.40	0.08	<.0001
Age80*Cohort 1902 to 1911				-0.05	0.01	<.0001	-0.04	0.009	0.00
Age80*Cohort 1912 to 1921				-0.02	0.01	0.00	-0.02	0.007	0.01
Age80*Cohort 1922 to 1931				-0.01	0.01	0.07	-0.02	0.007	0.045
Education <HS							-0.64	0.04	<.0001
Education =HS							-0.20	0.04	<.0001
Age80*Education <HS							-0.006	0.004	0.12
Age80*Education =HS							0.0006	0.004	0.86

Notes:
Reference groups: Male; Cohort 1932 to 1943; Age80*Cohort 1932 to 1943; age80*Education >HS.
Age variable was centered at age 80 (i.e., age at each assessment – 80).
Age and intercept are treated as random effects.

2D. Language (Category Fluency Animals)

	Model 1			Model 2			Model 3		
	Coeff.	**SE**	**P-Value**	**Coeff.**	**SE**	**P-Value**	**Coeff.**	**SE**	**P-Value**
Intercept	-0.17	0.02	<.0001	0.33	0.08	<.0001	0.45	0.08	<.0001
Female	-0.04	0.03	0.17	-0.05	0.03	0.11	-0.04	0.03	0.11
Age80	-0.05	0.002	<.0001	-0.03	0.01	0.00	-0.03	0.007	0.00
Cohort 1902 to 1911				-0.88	0.09	<.0001	-0.68	0.09	<.0001
Cohort 1912 to 1921				-0.62	0.08	<.0001	-0.49	0.08	<.0001
Cohort 1922 to 1931				-0.35	0.08	<.0001	-0.32	0.08	<.0001
Age80*Cohort 1902 to 1911				-0.05	0.01	<.0001	-0.04	0.009	<0.001
Age80*Cohort 1912 to 1921				-0.01	0.01	0.14	-0.01	0.008	0.11
Age80*Cohort 1922 to 1931				-0.01	0.01	0.52	-0.007	0.04	0.37
Education <HS							-0.49	0.04	<.0001
Education =HS							-0.19	0.04	<.0001
Age80*Education <HS							-0.002	0.004	0.52
Age80*Education=HS							-0.001	0.004	0.76

Notes:
Reference groups: Male; Cohort 1932 to 1943; Age80*Cohort 1932 to 1943; age80*Education >HS.
Age variable was centered at age 80 (i.e., age at each assessment – 80).
Age and intercept are treated as random effects.

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