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Birth Cohorts and Cognitive Reserve Influence Cognitive Performances in Older Adults

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Abstract.
Background: Evidence suggests birth cohort differences in cognitive performance of older adults. Proxies of cognitive reserve (CR), such as educational attainment and occupational complexity, could also partly account for these differences as they are influenced by the sociocultural environment of the birth cohorts.
Objective: To predict cognitive performance using birth cohorts and CR and examine the moderating influence of CR on cognitive performance and structural brain health association.
Methods: Using ADNI data ($n = 1628$), four birth cohorts were defined (1915–1928; 1929–1938; 1939–1945; 1946–1964). CR proxies were education, occupational complexity, and verbal IQ. We predicted baseline cognitive performances (verbal episodic memory; language and semantic memory; attention capacities; executive functions) using multiple linear regressions with CR, birth cohorts, age, structural brain health (total brain volume; total white matter hyperintensities volume) and vascular risk factors burden as predictors. Sex and CR interactions were also explored.
Results: Recent birth cohorts, higher CR, and healthier brain structures predicted better performance in verbal episodic memory, language and semantic memory, and attention capacities, with large effect sizes. Better performance in executive functions was predicted by a higher CR and a larger total brain volume, with a small effect size. With equal score of CR, women outperformed men in verbal episodic memory and language and semantic memory in all cohorts. Higher level of CR predicted better performance in verbal episodic memory, only when total brain volume was lower.
Conclusion: Cohort differences in cognitive performance favor more recent birth cohorts and suggests that this association may be partly explained by proxies of CR.

Keywords: Aging, birth cohorts, cognition, cognitive impairments, cognitive reserve, generations

[1]Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (http://adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. A complete listing of ADNI investigators can be found at: http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf

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INTRODUCTION

Cognitive aging is a heterogeneous process. A multitude of factors have been proposed to explain age-expected decline in cognitive performance in both normal [1, 2] and pathological cognitive aging (e.g., Alzheimer's disease (AD) [3, 4]), such as age-related cerebral volume loss [5] and cerebrovascular lesions (e.g., white matter hyperintensities (WMH)) [2], as well as late-life type 2 diabetes [6], midlife hypertension [7], obesity [8], and smoking [9]. Furthermore, it is observed that exposure to similar factors do not result in a similar cognitive decline in all individuals. Cognitive reserve (CR) may be a mechanism by which an individual cope with neurological changes induced by normal or pathological aging, allowing them to live longer without cognitive impairment [10, 11]. CR is expected to influence the association between brain pathology and clinical outcome, such that individuals with high CR cope better with neurodegenerative pathology [12, 13]. Proxies of CR have been reported to influence the onset of cognitive deficits and decrease the risk of dementia [14, 15]. Thus, higher educational attainment [16], occupations characterized by higher complexity in adulthood [17, 18] and higher verbal intellectual quotient (IQ) [19] have been independently associated with better cognitive performance in late life.

Although proxies of CR appear to be individual-centric, they are strongly influenced by the sociocultural environment that shaped the lives of these individuals. *Ipso facto* older adults from different age groups may have had different educational, professional, or cultural experiences throughout their lives [20] that could result in higher variance in their CR [21]. To examine the influence of broader sociocultural environment and its impact on CR and cognitive performance, the use of birth cohorts is indicated because they gather individuals who have shared common life experiences [20–22], which may have lasting effects on their cognitive function [23] and brain development [24].

Many studies investigating the impact of age on cognitive performance in late life do not consider year of birth [21, 25]. This is particularly problematic in multi-wave, longitudinal studies, where individuals of the same age are recruited over a long period of time and therefore from multiple birth cohorts [23]. It is then impossible to differentiate the influence of the sociocultural environment from that of age. Several studies have shown that later-born cohorts, when assessed at the same chronological age, tend to perform better than earlier-born cohorts on various cognitive tasks [26–29]. Munukka et al. [30] found similar cohort differences in participants assessed at age 75 and 80 for multiple cognitive outcomes. Higher educational attainment in the later-born cohorts explains much of the cohort differences for both men and women in phonemic verbal fluency (letter K; 3 min) at age 80, in processing speed (Digit Symbol) at age 75 and 80, and only in men at age 75 for short-term memory (Digit Span). Higher years of education and self-rated health were also found in later-born cohort (1938-1939 and 1942-1943) compared with the earlier-born cohort (1910 to 1914) [30], highlighting improvements in terms of education [23] and management of vascular risk factors, known to contribute to dementia, over the past century [21, 31]. In comparison to an earlier-born cohort (1920 to 1930), a later-born cohort (1931–1941) was shown to have better performance in global cognition (Mini-Mental State Examination), inductive reasoning (Raven Colored progressive matrices) and processing speed (Digit Symbol) at age 65 [32]. These differences were explained by education (except processing speed) [32]. Despite that, these results not only support the relevance of considering the sociocultural environment when studying cognition in aging, but also highlight the heterogeneity of operationalization across studies, as results depend on the cognitive domains being assessed and the tests being used [32]. Overall other sources of discrepancies between the studies are differences in 1) birth years (e.g., the Seattle Longitudinal Study cohorts were partly born earlier [27] than most other studies); 2) operationalization of birth cohorts (e.g., formed according to study's recruitment years [26, 27, 30, 32, 33]; 3) number of years covered in each cohort ranging from two [30] to 34 years [27]; 4) number of birth cohorts compared ranging from two [26, 27, 30, 32] to four [33]); and 5) sociocultural specificities regarding countries that may have undergone different societal changes during the last hundred years (e.g., United States [27, 33], Sweden [26], Netherlands [32], Finland [30]). Although some studies only control for age [26], most of them have included individual characteristics as covariates such as age, sex, and education [27, 29, 32–35], as well as the presence of self-reported chronic diseases (e.g., hypertension, cerebrovascular disease, cancer, etc.) [27, 32]. However, none have considered brain volume or WMHs burden nor have included proxies of CR other than education.

Our study aimed to examine birth cohort differences in factors underlying potential birth cohort differences, namely proxies of CR, with birth cohorts defined by major historical events that occurred during the first half of the 20th century. We also examined the role of birth cohorts and CR on cognitive performances, as well as the influence of measures of structural brain health and vascular risk factors burden. We hypothesized that individuals from more recent birth cohorts and with higher CR would show better cognitive performance than those born earlier and with lower CR. We also expected that a healthier brain structure (larger brain volume, lower WMH burden) and fewer vascular risk factors would also predict better cognitive performance. We further posited that CR would moderate the association between structural brain health and cognitive performance, where a higher CR would compensate the impact of lower brain volume and higher WMH burden on cognitive performances.

METHODS

Participants and birth cohorts

Data used in the preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database in May 2021. Launched in 2003 as a public-private partnership and led by Principal Investigator Michael W. Weiner, MD, the primary goal of ADNI is to test whether serial magnetic resonance imaging (MRI), positron emission tomography, other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment (MCI) and early AD. Approval from the local ethics board (CIUSSSCN #2021–2054) and written informed consent of the participants were obtained as part of the ADNI study. Recruited through 67 sites in the United States and Canada, participants were aged 55–90, were fluent in English or Spanish and had completed at least six grades of education. Participants undergo a series of initial tests that are repeated at intervals over subsequent years, including a clinical evaluation, neuropsychological tests, and MRI scan (for up-to-date information, see http://adni.loni.usc.edu/). The present study included participants with normal cognition (NC) with or without subjective memory complaints, MCI and AD. Diagnostic classification was made by ADNI clinical investigators using established research criteria for NC, MCI [36], and AD [3, 37]. At baseline, participants' demographics were obtained, including observed sex (recorded as men or women), year of birth, ethnicity, number of years of education, and main occupational attainment during adulthood. Birth cohorts were formed according to preexisting generations in the United States population census and to major historical events that have occurred in the United States and Canada [20]. They were classified as World War I, Spanish influenza pandemic and pre-Great Depression (≤ 1928), Great Depression (1929 to 1938), World War II (1939 to 1945), and post-World War II and Baby boom (≥ 1946).

Measures of cognitive reserve

Since composite proxies are likely to be a better representation of CR than single indicators [38, 39], we created a composite score of CR using the sum of scores of different validated proxies (i.e., education [40, 41], complexity of main occupational attainment during adulthood [42–44], and verbal IQ [45]), each coded into three categories (0, 1 or 2). With each score having the same weight, the CR score ranged from 0 to 6 with higher scores indicating a greater CR.

Education

The number of years of education was categorized into three levels based on the American educational system, as similarly done in previous studies [40, 41], where ≤ 12 years of education (high school and lower) were coded as 0, between 13 and 16 years (college and undergraduate programs) as 1, and ≥ 17 years (graduate programs and higher) as 2.

Occupational complexity

Previous studies have shown that the best way to assess the influence of occupational attainment on cognitive performances in older age is by judging it according to the relative complexity of its accomplishment [42–44]. Therefore, the complexity of main occupational attainment during adulthood was scored by three independent raters (VT and two other) using the ten major groups of the International Standard Classification of Occupations 2008 (ISCO-08) [46], as previously published [42]. As recommended by the ISCO-08, we have classified military works into a group of similar civilian jobs since the armed forces have jobs of varying complexities. Therefore, only low-skill military jobs (e.g., physical or manual) were classified as "Armed Forces Occupations" (group 10; representing Major Group 0 in the ISCO-08 but renamed as group 10 to fit

hierarchical skill levels). Participants who have never had a job (e.g., housewives, househusbands) were classified as "Elementary occupations" (group 9). Briefly, group 1 corresponds to the most complex jobs and group 10 corresponding to the least complex jobs (Supplementary Table 1 for details). Cohen's kappa was used to assess inter raters' reliability, with a resulting estimate averaged across coder pairs of 0.719 (rater pair kappa estimates = 0.695 [raters 1 and 2], 0.765 [raters 2 and 3], and 0.696 [raters 1 and 3]), indicating substantial agreement according to Landis and Koch [47]. The major occupational groups were then categorized into three levels according to skill levels also described in the ISCO-08 (from 1 to 4, with higher score indicating a greater skill level), where groups 1 and 2 (skill level 4) were coded as 2, group 3 (skill level 3) as 1 and groups 4 to 10 (skill levels 1 and 2) as 0.

Verbal intellectual quotient

Verbal IQ was estimated using the American version of the National Adult Reading Test [48]. The number of errors made was transformed into an estimated verbal IQ using the formula of Grober and Sliwinski [49], as previously done [45]. Estimated verbal IQ was categorized in three levels based on standard IQ mean and standard deviation ($M = 100$, $SD = 15$) [50], where estimates ≤ 115 (average: –1 to 1 SD) were coded as 0, between 116–123 (above average: 1 to 1.5 SD) as 1 and ≥ 124 (high above average: > 1.5 SD) as 2.

Measures of structural brain health

Anatomical brain measurements were obtained from a standardized, high-quality, 3D volumetric T1-weighted acquisition on either 1.5 or 3 Tesla MRI (Siemens Medical Solutions, Philips Medical Systems or General Electric Healthcare) [51]. Baseline total brain volumes, an indicator of global brain anatomy, were derived from these T1-weighted images using the "recon-all -all" command of *FreeSurfer* 6.0 (http://freesurfer.net) [52] on the raw images with the fully automated directive parameters (no manual intervention or expert flag options) on the CBRAIN platform [53]. We then transformed total volumes into z-scores, adjusting for estimated total intracranial volume, scanner manufacturer, magnetic field strength, image resolution and image quality, as per the process defined in Potvin et al. [54] and based on normative data from 6,909 healthy individuals.

WMHs were used as proxies of cerebrovascular burden. WMHs are typically assessed using Fluid-attenuated Inversion Recovery (FLAIR) or dual T2-weighted and proton density scans, which have optimum contrast for detecting such lesions. However, as FLAIR sequence was not included in ADNI until 2010, this would have substantially reduced our sample size. We therefore used a previously validated segmentation technique to automatically segment WMHs from T1-weighted images using a set of intensity and spatial features and a Random Forest classifier [55, 56]. Although WMH volumes obtained from T1-weighted are smaller than FLAIR volumes, they are still able to retain high correlations in all brain regions ($r = 0.96$) [55]. Total WMH volumes were calculated in the stereotaxic space to make population comparisons possible. Because of abnormal distribution with a positive skewness, raw volumes were log-transformed.

Measures of vascular risk factors burden

At baseline physical examination, participants had a blood draw after 6 h fasting overnight to extract fasting plasma glucose levels. A diagnosis of type 2 diabetes was based on a fasting plasma glucose reading ≥ 126 mg/dL [57]. Systolic and diastolic blood pressures were also taken in a sitting position. Hypertension was diagnosed based on a high systolic (≥ 130 mm Hg) or diastolic (≥ 80 mm Hg) reading [58]. Participants' height and weight were also collected. Obese range was determined by a body mass index ≥ 30 kg/m^2 [59]. Lifetime smoking history (past or current smoker) was also recorded.

A vascular index score was calculated by summing four dichotomous variables created for the four vascular risk factors mentioned above (each coded as 0 = absent versus 1 = present), as previously published [60–62]. The vascular index was multiplied by –1, ranging from 0 to –4 with lower negative scores corresponding to a higher vascular risk factors' burden. Since vascular risk factors seldom occur in isolation, using a combined score is likely to improve sensitivity in detecting their impacts [60].

Measures of cognitive performance

Cognitive performance (our dependent variable) was evaluated using ten neuropsychological tests, representing four cognitive domains. Verbal episodic memory was assessed with the Mini-Mental State Examination (three words delayed recall), the

Logical Memory I and II (number of elements correctly recalled for story A, immediate and delayed conditions) of the Wechsler Memory Scale, the Rey Auditory Verbal Learning Test (15 words recalled in five learning trials, after interference list and after delay) and three subtests of the Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog), namely Word recall, Delayed free recall and Word recognition. Language and semantic memory were assessed with the subtest Naming Objects and Fingers (number of objects [maximum 12] and fingers [maximum 5] named) of the ADAS-Cog and with Semantic verbal fluency test (number of animals named in one minute). Attention capacities were assessed with the time required to complete the Trail Making Test (TMT) Part A (150 s maximum) and with the subtest Number Cancellation (49 target hits maximum) of the ADAS-Cog. Finally, executive functions were assessed with the ratio of the time to complete the TMT Part B (300 s maximum) divided by the time to complete Part A (B/A). This ratio reduce the influence of speed and isolate the additional time associated to the task switching cost of Part B [63].

In order to maximize reliability and generalizability [25], for each cognitive domain, a composite score was created by averaging the z-scores from each test, except for verbal episodic memory. TMT scores were multiplied by –1 since higher score meant lower performance. Because of a negatively skewed distribution, TMT B/A ratio was reflected and log-transformed before calculating the z-scores. For verbal episodic memory, Crane et al. [64] composite z-score was used since it accounts for different versions of the Rey Auditory Verbal Learning Test administered through ADNI, with the second version being more difficult than the first [64]. The latter was then transformed in z-score based on the mean and standard deviation of the study sample.

Statistical analyses

Descriptive statistics for participants' characteristics were carried out for the total sample and across birth cohorts. To identify significant differences between the birth cohorts, one-way ANOVAs and Tukey's test for *post-hoc* analyses were performed. Sex differences across birth cohorts on CR score and individual proxies' scores (education; complexity of occupation; verbal IQ) was assessed through factorial ANOVAs. When sex and birth cohorts' interactions were statistically significant, one-way ANOVAs were conducted for women and men separately. The normed scores of total brain volume and the log-transformed total WMH volume were transformed in z-scores based on the mean and standard deviation of the study sample. Linear regressions were conducted to predict each cognitive domain composite scores (i.e., verbal episodic memory; language and semantic memory; attention capacities; executive functions) with age, birth cohorts, CR, structural brain health (total brain volume; total WMH volume), and vascular index as predictors. Dummy coding was applied to birth cohorts with the earliest birth cohort (1915 to 1928) as the reference. To investigate the potential moderation influence of CR on structural brain health and cognitive performance association, the interactions between total brain volume and CR (Brain x Cognitive reserve) and between total WMH volume and CR (WMH x Cognitive reserve) were tested. The interaction between gender and CR was also investigated. For significant Sex x Cognitive reserve interactions, a separated regression model for men and women was performed. All statistical analyses were conducted using SPSS Statistics 26.0 (IBM Corp., Armonk, NY) and tested with an alpha level of 0.05. Inspection of the residuals was done to ensure that the linear regression assumptions were met.

RESULTS

Sociodemographics

We excluded a total of 72 participants as they were missing one of the main variables (Table 1). Participants included in the present study were similar to the excluded group in terms of age ($M = 73.5$, SD = 7.2 in our final sample versus $M = 71.5$ years, SD = 7.8 in the excluded sample; $p = 0.502$), sex (47.4%, $n = 771$ versus 48.6% women, $n = 35$; $p = 0.747$), year of birth ($M = 1937$, SD = 9.4 versus $M = 1941$, SD = 9.5; $p = 0.780$), years of education ($M = 16.1$, SD = 2.8 versus $M = 15.0$, SD = 3.3; $p = 0.094$), and on diagnostic (43.5% MCI and 17.3% AD versus 29.2% MCI and 54.2% AD; $p = 0.152$).

Descriptive statistics for all demographic and clinical variables are provided in Table 2. The study sample consisted of 1,628 participants, of whom 91.8% were white, with most participants born in the 1929–1938 cohort. A large proportion of participants achieved a high educational level (42.2% had ≥ 17 years of education), held more complex jobs (58.8% classified in the ISCO-08's groups 1 and 2; Supplementary Table 1) and had verbal IQ estimates well above average (29.1% had estimates ≥ 124).

Table 1
Flowchart of participants included in analyses

	Total	NC	MCI	AD
Participants with ADNI baseline T1-weighted MRI scans that passed segmentation quality control	1,700	651	729	320
↓				
Excluded participants with missing neuropsychological data	47	3	13	31
↓				
Excluded participants with missing cognitive reserve data	25	9	8	8
↓				
Final analyses	**1,628**	**639**	**708**	**281**

ADNI, Alzheimer's Disease Neuroimaging Initiative; MRI, magnetic resonance imaging; NC, normal cognition; MCI, mild cognitive impairment; AD, Alzheimer's disease.

Comparisons across all birth cohorts showed that participants from the most recent birth cohort were younger ($p < 0.0001$), were mainly women ($p < 0.0001$; 23.5% more in 1946–1964 versus 1915–1928), had more years of education ($p < 0.0001$) and higher verbal IQ estimates ($p = 0.001$). The most recent birth cohort (1946–1964) gained, on average, one year of education and 2.2 units of verbal IQ estimate compared to the earliest born cohort (1915–1928). Participants born more recently showed a healthier brain structure, suggested by a larger total brain volume ($p < 0.0001$) and a lower total WMH volume ($p < 0.0001$), compared to those born earlier. Out of 1,628 participants, 497 (30.5%) had missing data in at least one of the factors of the vascular index but were still included in the final analyses. For these participants, missing data were coded as 0 (absence of the vascular risk factor) in the computation of the vascular index. Two or more vascular risk factors were present in 28.5% of the participants, whereas 30.6% had none. Comparisons between all birth cohorts revealed a decrease in hypertension ($p = 0.002$; 10.2% lower in 1946–1964 versus 1915–1928) and an increase in obesity ($p < 0.0001$; 12.1% higher in 1946–1964 versus 1915–1928). Although there appeared to be a decrease, no statistically significant difference between all birth cohorts was observed for type 2 diabetes (8.4% less in 1946–1964 versus 1915–1928) and smoking (26.5% less in 1946–1964 versus 1915–1928).

Cognitive reserve across birth cohorts

Birth cohorts' influence on CR score and proxies are reported in Table 3. Statistically significant differences between birth cohorts were found for CR ($p < 0.0001$), education score ($p < 0.0001$), complexity of occupation score ($p = 0.004$) and verbal IQ score ($p = 0.002$). *Post-hoc* comparisons revealed that participants born in the most recent cohort (1946 to 1964) compared to those born in the two earliest birth cohorts (1915–1928; 1929–1938) had greater CR ($p < 0.0001$; $p = 0.005$), were more educated ($p < 0.0001$; $p = 0.023$) and had a higher verbal IQ ($p = 0.011$; $p = 0.001$). They held more complex occupation compared to the earliest birth cohort (1915–1928; $p = 0.002$). Participants born during World War II (1939–1945) were more educated than those born during the earliest cohort ($p = 0.042$). Those born during the Great Depression (1929–1938) held more complex occupation than those born in the earliest cohort ($p = 0.045$).

Cognitive reserve across sex and birth cohorts

Significant differences between men and women were observed for CR ($p < 0.0001$), education score ($p < 0.0001$) and complexity of occupation score ($p < 0.0001$), but not for verbal IQ score ($p = 0.386$). Significant interaction between sex and birth cohorts were found for CR ($p = 0.011$) and complexity of occupation's score ($p < 0.0001$), but not for education score ($p = 0.063$) and verbal IQ score ($p = 0.881$). Means and standard deviations of scores of CR and its proxies are reported in Table 3. Between-group comparisons in men revealed no main effect of birth cohorts for scores of CR and complexity of occupation ($p \geq 0.441$). In women, between-group comparisons revealed a significant influence of birth cohorts for CR ($p < 0.0001$) and complexity of occupation score ($p < 0.0001$). *Post-hoc* comparisons revealed that women born in the most recent cohort (1946–1964) had greater CR ($p \leq 0.018$) compared to all previous cohorts. Compared to the two earliest birth cohorts (1915–1928 and 1929–1938), they also held more complex jobs ($p \leq 0.002$). Women born

Table 2
Baseline characteristics[a] of participants, by birth cohorts

	All	Birth Cohorts				*p*
		1915–1928 (World War I, Spanish influenza, pre-Great Depression)	1929–1938 (Great Depression)	1939–1945 (World War II)	1946–1964 (post-World War II, Baby boom)	
	N = 1,628	*N* = 338	*N* = 628	*N* = 320	*N* = 342	
Age (y)	73.5 (7.2)	82.4 (3.2)	75.2 (4.0)	70.3 (4.5)	64.8 (4.5)	< 0.0001
Year of birth (y)	1937 (9.4)	1924 (3.0)	1934 (2.7)	1942 (2.0)	1950 (3.7)	
Women	771 (47.4%)	124 (36.7%)	282 (44.9%)	159 (49.7%)	206 (60.2%)	< 0.0001
Baseline diagnostic						
Normal cognition	639 (39.3%)	90 (26.6%)	235 (37.4%)	126 (39.4%)	188 (55.0%)	
Mild cognitive impairment	708 (43.5%)	161 (47.6%)	275 (43.8%)	149 (46.6%)	123 (36.0%)	
Alzheimer's disease	281 (17.3%)	87 (25.7%)	118 (18.8%)	45 (14.1%)	31 (9.1%)	
Cognitive reserve score	3.5 (1.9)	3.3 (1.9)	3.5 (1.9)	3.6 (1.9)	3.9 (1.7)	
Education (years)	16.1 (2.8)	15.6 (3.1)	16.0 (2.8)	16.1 (2.7)	16.6 (2.4)	< 0.0001
0: High school and lower, ≤ 12	238 (14.6%)	69 (20.4%)	95 (15.1%)	44 (13.8%)	30 (8.8%)	
1: College and undergraduate, 13–16	703 (43.2%)	145 (42.9%)	276 (43.9%)	134 (41.9%)	148 (43.3%)	
2: Graduate, ≥ 17	687 (42.2%)	124 (36.7%)	257 (40.9%)	142 (44.4%)	164 (48.0%)	
Estimated verbal IQ	117.7 (9.5)	117.2 (9.6)	116.9 (9.8)	117.7 (9.3)	119.4 (8.6)	0.001
0: Average, ≤ 115	578 (35.5%)	132 (39.1%)	241 (38.4%)	110 (34.4%)	95 (27.8%)	
1: Above average, 116–123	577 (35.4%)	111 (32.8%)	221 (35.2%)	120 (37.5%)	125 (36.5%)	
2: High above average, ≥ 124	473 (29.1%)	95 (28.1%)	166 (26.4%)	90 (28.1%)	122 (35.7%)	
ISCO-08 complexity of occupation						
0: Skill levels 1-2, groups 4–10	429 (26.4%)	108 (32.0%)	165 (26.3%)	86 (26.9%)	70 (20.5%)	
1: Skill level 3, group 3	241 (14.8%)	56 (16.6%)	80 (12.7%)	51 (15.9%)	54 (15.8%)	
2: Skill level 4, groups 1-2	958 (58.8%)	174 (51.5%)	383 (61.0%)	183 (57.2%)	218 (63.7%)	
Vascular index[b]	–1.4 (0.9)	–1.4 (0.8)	–1.4 (0.9)	–1.2 (0.9)	–1.4 (1.0)	0.071
Hypertension	1,069 (65.7%)	240 (71.0%)	429 (68.3%)	192 (60.0%)	208 (60.8%)	0.002
Obesity[c]	303 (18.6%)	48 (14.2%)	105 (16.7%)	60 (18.8%)	90 (26.3%)	< 0.0001
Type 2 diabetes[d]	97 (6.0%)	35 (10.4%)	44 (7.0%)	11 (3.4%)	7 (2.0%)	0.143
Ever smoked[e]	513 (31.5%)	137 (40.2%)	240 (38.2%)	89 (27.8%)	47 (13.7%)	0.704
Structural brain measures (Z scores)						
Total brain volume	0.0 (1.0)	–0.7 (0.8)	–0.2 (0.9)	0.3 (0.9)	0.8 (0.9)	< 0.0001
Total WMH volume[f]	0.0 (1.0)	0.6 (1.1)	0.1 (1.0)	–0.3 (0.8)	–0.6 (0.6)	< 0.0001
Cognitive performances (Z scores)						
Verbal episodic memory	0.0 (1.0)	–0.4 (0.9)	–0.1 (1.0)	0.2 (1.0)	0.4 (0.9)	< 0.0001
Language and semantic memory	0.0 (0.8)	–0.3 (0.8)	–0.1 (0.8)	0.1 (0.6)	0.4 (0.6)	< 0.0001
Attention capacities	0.0 (0.9)	–0.4 (0.8)	–0.1 (0.9)	0.2 (0.8)	0.3 (0.8)	< 0.0001
Executive functions	0.0 (1.0)	–0.2 (1.0)	–0.0 (1.0)	0.1 (1.0)	0.1 (0.9)	< 0.0001

Differences between birth cohorts were examined by ANOVAs for continuous variables and with Kruskal-Wallis for categorical variables. IQ, intellectual quotient; ISCO-08, International Standard Classification of Occupations 2008; WMH, white matter hyperintensities. [a] Values shown are mean (standard deviation) or number (percentage); [b] 497 missing values; [c] 2 missing values; [d] 496 missing values; [e] 357 missing values; [f] Negative Z scores mean lower WMH burden.

Table 3
Means, standard deviations, and one-way analyses of variance in cognitive reserve score (0 to 6) and proxies' scores (0 to 2) across birth cohorts

Variable	1915–1928		1929–1938		1939–1945		1946–1964		$F(3, 1624)$[a]	p
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*		
Cognitive reserve										
Women	2.71	1.95	3.20	1.90	3.36	1.89	3.94	1.72	12.50	****
Men	3.56	1.88	3.72	1.84	3.73	1.88	3.85	1.73	0.72	0.541
Total	3.25	1.95	3.49	1.89	3.55	1.89	3.90	1.72	7.24	****
Education										
Women	1.02	0.74	1.12	0.69	1.21	0.69	1.39	0.66		
Men	1.25	0.73	1.37	0.69	1.40	0.70	1.40	0.62		
Total	1.16	0.74	1.26	0.70	1.31	0.70	1.39	0.64	6.44	****
Complexity of occupation										
Women	0.81	0.91	1.16	0.90	1.21	0.90	1.45	0.80	13.96	****
Men	1.42	0.81	1.50	0.81	1.39	0.83	1.41	0.83	0.90	0.441
Total	1.20	0.89	1.35	0.87	1.30	0.87	1.43	0.81	4.55	**0.004**
Verbal IQ										
Women	0.89	0.78	0.92	0.80	0.94	0.77	1.11	0.79		
Men	0.89	0.84	0.85	0.80	0.93	0.82	1.04	0.80		
Total	0.89	0.81	0.88	0.80	0.94	0.79	1.08	0.79	5.03	**0.002**

****$p < 0.0001$. $N = 1{,}628$. IQ, intellectual quotient. [a]One-way ANOVAs for women ($n = 771$), $F(3, 767)$; One-way ANOVAs for men ($n = 857$), $F(3, 853)$.

during World War II (1939–1945) have greater CR ($p = 0.018$) and held more complex jobs ($p = 0.001$) compared to the earliest cohort (1915–1928). Women born during the Great Depression (1929–1938) held more complex jobs ($p = 0.001$) compared to those born in the earliest cohort (1915–1928).

Prediction of cognitive performance

Variables predicting each cognitive performance score are reported in Table 4. The models explained 28.2% of the variance for verbal episodic memory, 20.8% for language and semantic memory, 20.3%

Table 4
Linear regression analyses for variables predicting cognitive performance in four cognitive domains ($N = 1628$)

	Verbal episodic memory			Language and semantic memory			Attention capacities			Executive functions		
Predictors	*B*	*SE B*	*p*	*B*	*SE B*	*p*	*B*	*SE B*	*p*	*B*	*SE B*	*p*
(Intercept)	–3.26	0.45	****	–1.30	0.36	****	–2.34	0.41	****	–0.46	0.51	0.368
Age	0.03	0.01	****	0.01	0.00	**0.033**	0.02	0.00	****	0.00	0.01	0.944
Birth cohorts[a]												
1915–1928												
1929–1938	0.22	0.07	**0.001**	0.17	0.06	**0.002**	0.24	0.06	****	0.06	0.08	0.469
1939–1945	0.46	0.09	****	0.32	0.07	****	0.44	0.09	****	0.08	0.11	0.441
1946–1964	0.62	0.12	****	0.48	0.09	****	0.54	0.11	****	0.02	0.13	0.906
Cognitive reserve[b]	0.18	0.01	****	0.12	0.01	****	0.08	0.01	****	0.11	0.02	****
Total brain volume	0.41	0.05	****	0.19	0.04	****	0.29	0.05	****	0.15	0.06	**0.010**
Total WMH volume	–0.11	0.05	**0.021**	–0.09	0.04	**0.013**	–0.13	0.04	**0.002**	–0.03	0.05	0.553
Vascular index[c]	–0.02	0.02	0.401	–0.02	0.02	0.387	–0.00	0.02	0.969	0.00	0.03	0.971
Brain × Cognitive reserve	–0.03	0.01	**0.016**	–0.01	0.01	0.171	–0.01	0.01	0.259	–0.01	0.01	0.617
WMH × Cognitive reserve	–0.01	0.01	0.451	0.01	0.01	0.229	–0.00	0.01	0.916	–0.00	0.01	0.740
Sex × Cognitive reserve	–0.08	0.01	****	–0.03	0.01	****	–0.02	0.01	0.068	–0.00	0.01	0.986

****$p < 0.0001$. All outcomes presented as Z scores. Sex (men = 1, women = 0). WMH, white matter hyperintensities. [a] 1915–1928 is the reference. 1929–1938, 1939–1945 and 1946–1964 : 1 = born in this cohort, 0 = born in another cohort. [b] Cognitive reserve score ranging from 0 (low reserve) to 6 (high reserve). [c] Vascular index ranging from 0 (no vascular risk factor burden) to –4 (high vascular risk factors burden).

for attention capacities, and 7.2% for executive functions. The effect sizes of associations were all large, with the exception of executive functions which was small. CR and total brain volume contributed significantly to all models. Birth cohorts, age, and total WMH volume contributed significantly to predict performances in verbal episodic memory, language and semantic memory, and attention capacities. The vascular index did not significantly predict cognitive performance in any models. We further tested the non-linear effect of the aging process and results showed statistically significant contribution of age squared in all models (Supplementary Table 2; Supplementary Figure 1). Compared to the reference birth cohort (1915 to 1928), the regression coefficients increase as the birth cohorts become more recent. As for the CR score, the higher it was, the higher the performance scores were in all cognitive domains. In order to test the interaction between birth cohorts and CR in a parsimonious way, we reduced the number of categories of birth cohorts using a single dummy variable (0 = 1915 to 1938, 1 = 1939–1964) which allowed to be added to the model. Results showed no interaction between birth cohorts and CR for any prediction (Supplementary Table 3).

Cognitive performance across diagnoses

Previous studies have reported that higher CR delays the onset of AD, but once diagnosed with AD, individuals with higher CR declined more

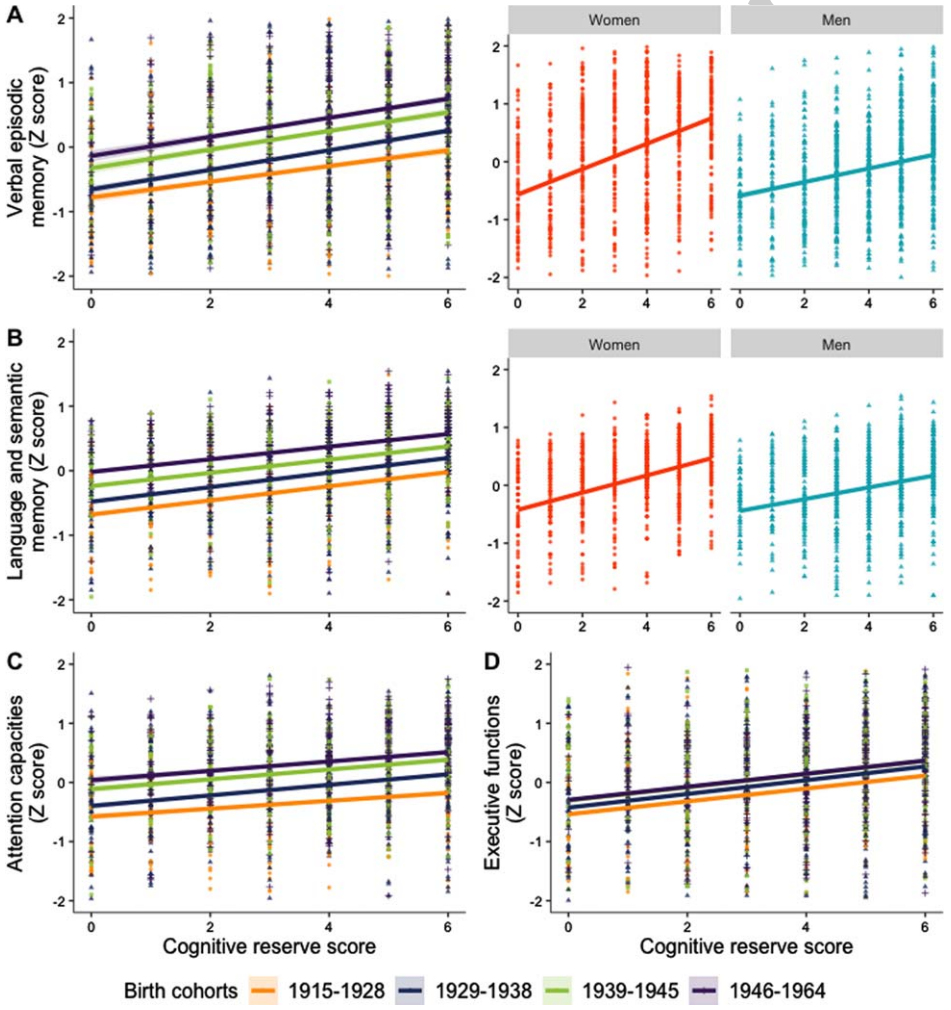

Fig. 1. Prediction of cognitive performance scores by cognitive reserve's score across birth cohorts and sex. 95% confidence intervals are shown as shaded areas around the regression lines.

rapidly than those with lower CR (e.g., [65]). Henceforth, we conducted subgroup analyses for each of the cognitive groups (NC, MCI, AD; Supplementary Figure 2). The results in MCI participants (n = 708; Supplementary Table 5) were nearly similar to those obtained with the whole sample, where more recent birth cohorts performed better than the earlier cohort (except for executive functions). The influence of birth cohorts was only observed in predicting attention capacities in AD participants (n = 281; Supplementary Table 6), whereas only in predicting verbal episodic memory in NC participants (n = 693; Supplementary Table 4). Higher CR predicted better performances in all cognitive domains for non-demented participants, while only in verbal episodic memory and executive functions for AD participants. In both clinical groups (MCI and AD), higher total brain volume predicted better performances in verbal episodic memory and attention capacities.

Sex and cognitive reserve moderation roles

There was a significant interaction between sex and CR in predicting verbal episodic memory, and language and semantic memory (Table 4), where, for equal CR scores, women outperformed men in all birth cohorts (Fig. 1). Results are shown in Table 5 for women and in Table 6 for men. In predicting verbal episodic memory, the model explained 27.3% of variance in women and 25.7% in men. Age, birth cohorts, CR and total brain volume contributed significantly to predict verbal episodic memory performances in both sexes. Total WMH volume contributed significantly to the model only in women. In predicting language and semantic memory, the model explained 22.7% of the variance in women and 18.6% in men. CR and total brain volume contributed significantly to predict language and semantic memory performances in both sexes. In women, age, more recent birth cohorts 1939–1945 and 1946–1964, and total WMH volume contributed significantly to the model. In men, all birth cohorts contributed significantly to the model, while total WMH volume did not. In either women or men models, vascular index did not contribute significantly to any prediction. Finally, CR only moderated the association between total brain volume and verbal episodic memory in men.

Regarding the moderation role of CR in the association between structural brain health and cognitive function, CR only moderated the association between total brain volume and verbal episodic memory performance (B = –0.03, p = 0.016), while the other interactions were not found statistically significant. As shown in Fig. 2, when total brain volume is low, individuals with high CR (score between 5 and 6) have better verbal episodic memory than those with moderate (score between 3 and 4) or low (score between 0 and 2) CR. In contrast, when total brain volume is large, having a high, moderate, or low CR does not seem to significantly influence verbal episodic memory.

Table 5
Linear regression analyses for variables predicting cognitive performance in Women (n = 771)

	Verbal episodic memory			Language and semantic memory		
Predictors	*B*	*SE B*	*p*	*B*	*SE B*	*p*
(Intercept)	–3.44	0.68	****	–1.54	0.50	**0.002**
Age	0.04	0.01	****	0.01	0.01	**0.019**
Birth cohorts[a]						
1915–1928						
1929–1938	0.28	0.11	**0.014**	0.11	0.08	0.187
1939–1945	0.45	0.15	**0.002**	0.24	0.11	**0.028**
1946–1964	0.69	0.18	****	0.40	0.13	**0.002**
Cognitive reserve[b]	0.14	0.02	****	0.12	0.01	****
Total brain volume	0.45	0.07	****	0.20	0.05	****
Total WMH volume	–0.15	0.07	**0.037**	–0.15	0.05	**0.005**
Vascular index[c]	–0.01	0.04	0.904	0.01	0.03	0.631
Brain x Cognitive reserve	–0.02	0.02	0.398	–0.01	0.01	0.363
WMH x Cognitive reserve	0.01	0.02	0.472	0.02	0.01	0.097

****p < 0.0001. All outcomes presented as Z scores. WMH, white matter hyperintensities. [a] 1915–1928 (n = 124) is the reference. 1929–1938 (n = 282), 1939–1945 (n = 159) and 1946–1964 (n = 206): 1 = born in this cohort, 0 = born in another cohort. [b] Cognitive reserve score ranging from 0 (low reserve) to 6 (high reserve). [c] Vascular index ranging from 0 (no vascular risk factor burden) to –4 (high vascular risk factors burden).

Table 6
Linear regression analyses for variables predicting cognitive performance in Men ($n = 857$)

	Verbal episodic memory			Language and semantic memory		
Predictors	*B*	*SE B*	*p*	*B*	*SE B*	*p*
(Intercept)	–3.17	0.58	****	–1.08	0.51	**0.035**
Age	0.03	0.01	****	0.01	0.01	0.439
Birth cohorts[a]						
1915–1928						
1929–1938	0.19	0.09	**0.030**	0.20	0.08	**0.007**
1939–1945	0.47	0.12	****	0.37	0.10	****
1946–1964	0.57	0.15	****	0.55	0.13	****
Cognitive reserve[b]	0.14	0.02	****	0.10	0.01	****
Total brain volume	0.37	0.07	****	0.18	0.06	**0.003**
Total WMH volume	–0.05	0.06	0.394	–0.04	0.05	0.424
Vascular index[c]	–0.04	0.03	0.224	–0.04	0.03	0.144
Brain x Cognitive reserve	–0.03	0.02	**0.041**	–0.01	0.01	0.317
WMH x Cognitive reserve	–0.03	0.02	0.058	0.00	0.01	0.894

****$p < 0.0001$. All outcomes presented as Z scores. WMH, white matter hyperintensities. [a] 1915–1928 ($n = 214$) is the reference. 1929–1938 ($n = 346$), 1939–1945 ($n = 161$) and 1946–1964 ($n = 136$): 1 = born in this cohort, 0 = born in another cohort. [b] Cognitive reserve score ranging from 0 (low reserve) to 6 (high reserve). [c] Vascular index ranging from 0 (no vascular risk factor burden) to –4 (high vascular risk factors burden).

DISCUSSION

In this study, we investigated the differences in cognitive performances in 1628 participants aged 55 to 90 years at baseline across birth cohorts defined by major historical events—those born between 1915 and 1928 (reference group; World War I, Spanish influenza pandemic and pre-Great Depression), 1929 and 1938 (Great Depression), 1939 and 1945 (World War II), and 1946 and 1964 (post-World War II and Baby boom). The specific contributions of CR, birth cohorts, age, structural brain health and vascular risk factors burden were examined, as well as the potential moderator role of CR in the association between brain structure and cognitive performance. In line with our hypotheses, results revealed that more recent birth cohorts, higher CR and healthier brain structures predicted better performance in verbal episodic memory, language and semantic memory, and attention capacities, whereas better performance in executive functions was predicted by a higher CR and a larger total brain volume. Indeed, greater CR (i.e., higher education, higher complexity of occupational attainment, higher verbal IQ) predicted significantly better performance in all cognitive domains, with up to 0.18 SD per unit of CR (total of 6) added to cognitive performance z-score. CR was the third most important predictor for verbal episodic memory and language and semantic memory, and the most important for executive functions, whereas it was the fifth for attention capacities. As for birth cohorts, the more recent they were, the better the cognitive performance. Cohort born between 1929 and 1938, between 1939 and 1945, and between 1946 and 1964 had cognitive performance that was respectively 0.24 SD, 0.46 SD, and 0.62 SD higher than the earliest cohort (1915–1928). The most recent birth cohort (1946–1964) followed by the birth cohort 1939–1945 were the most important predictors of performance in all cognitive domains, except for executive functions. Interactions between sex and CR were observed in verbal episodic memory, and language and semantic memory, with women outperforming men in all birth cohorts at equal CR. As expected, we found that, in participants with lower brain volumes, a high CR predicted better performance in verbal episodic memory than moderate or low CR; the magnitude of CR did not matter when total brain volume was larger.

The identification of birth cohort effects (characteristics restricted to a group of individuals born at the same time), which should be investigated by distinguishing them from age effects (characteristics associated with aging regardless of date of birth) and period effects (characteristics associated with living during a specific historical period, perhaps related to an exposure that occurred only during that time) [34, 66], could shed light on cohort-specific factors contributing to the interindividual variability reported in cognitive performance and decline [21, 31]. The birth cohort into which the individual was born represents the influence of the sociocultural environment

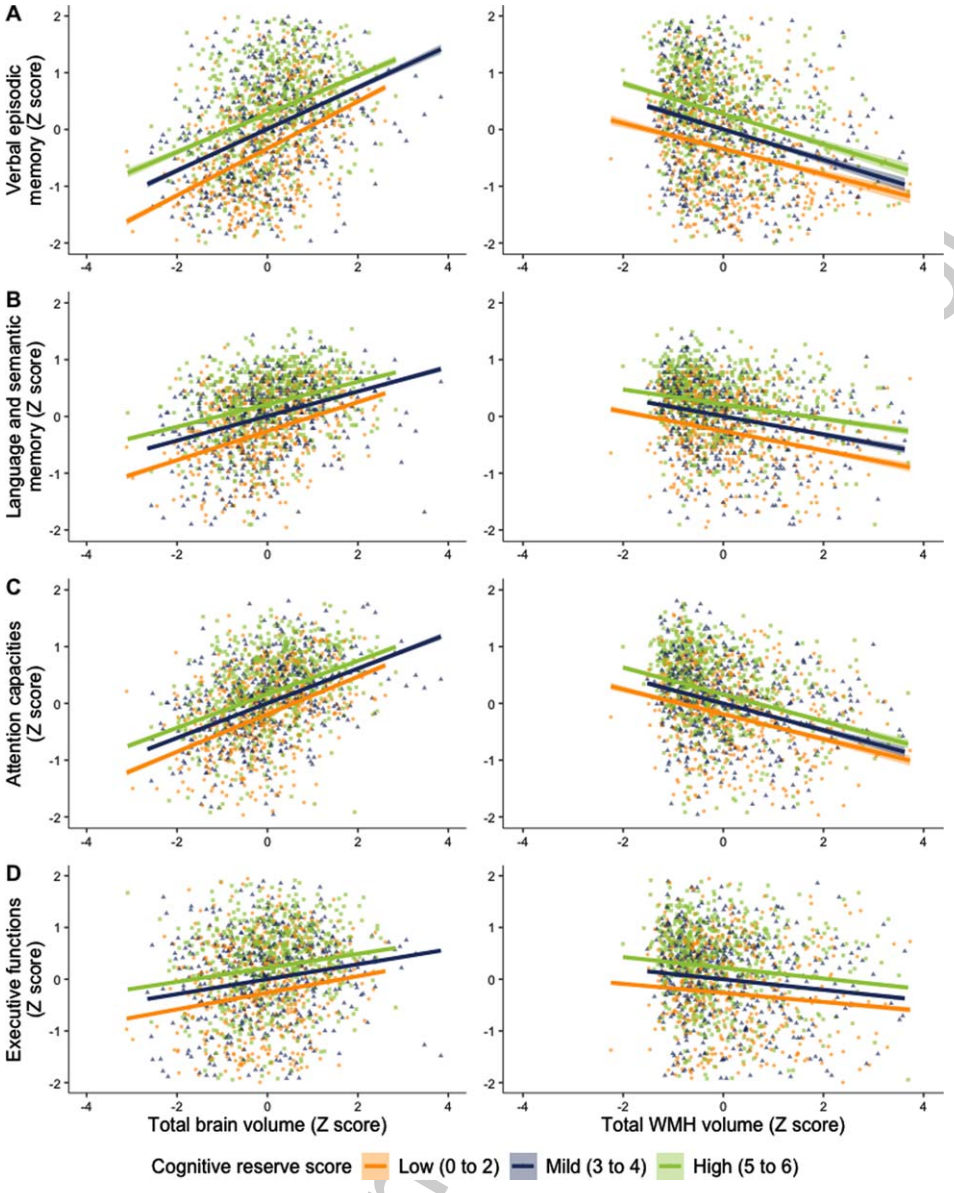

Fig. 2. Prediction of cognitive performance scores by brain measures across cognitive reserve's score. 95% confidence intervals are shown as shaded areas around the regression lines. WMH, white matter hyperintensities.

on childhood development. Subsequent years of life (i.e., adolescence, adulthood) may belong to this same cohort as well as to subsequent cohorts. This must be taken into account when interpreting the results of studies of birth cohort differences. Furthermore, historical cohorts or generational improvements in cognitive performance do not outweigh the negative influences of aging-related factors. Instead, cohort differences may be seen as a proxy for moderating variables [27] that best influence cognitive performance in later life, such as CR. Hence, having birth cohorts and CR associated with cognitive performance is consistent with the CR hypothesis [11], which suggests that other factors may contribute to explaining the gap between the pathology and cognitive functioning.

Domain-specific differences between birth cohorts in cognitive performance

Our results corroborate past findings showing domain-specific differences between birth cohorts in older individuals' cognitive performance (e.g., verbal episodic memory [34, 35]; language and semantic memory [27, 29, 33, 35]; attention capacities [29, 30, 32, 33]), but were also inconsistent with previous studies (e.g., verbal episodic memory [32]; attention capacities [26]; executive functions [27, 30, 33]). In these latter studies, design and heterogeneity of measurements may have led to discrepancies with our findings. Thus, cohort differences in attention capacities performance found in the present study were previously observed using tests of processing speed (e.g., Digit Symbol, TMT Part A) [29, 30, 32, 33], but were not present while using a combination of two tests (i.e., Digit Symbol and Figure identification), without adjustment for education [26]. Also, in disagreement with our finding, past studies reported that later-born cohorts outperformed earlier-born cohorts in executive functions, but these studies mainly assessed this cognitive domain with a phonemic verbal fluency test [27, 30, 33]. Although one of the latter studies [33] assessed executive functions with a second measure similar to ours (i.e., TMT Part B), a significant birth cohort influence was still found. Regarding verbal episodic memory performance, Brailean et al. [32] found opposite results to ours in participants aged 65 to 75, with the earlier born cohort (1920 to 1930) performing better than a later born cohort (1931–1941) in immediate recall (no differences in delayed recall) on the Dutch version of the Rey Auditory Verbal Learning Test, after adjusting for education. Many factors may explain this discrepancy such as a memory test with more familiar words for the earlier born cohort [32], difference in the administration of the test between the two birth cohorts (1995 versus 2005) and changes in the Dutch education system from rote learning for earlier-born cohort to discovery and active learning for later-born cohorts [67].

Cognitive reserve as a moderator in structural brain health and cognitive performance association

In our study, CR acted as a moderator in the association between total brain volume and verbal episodic memory performance. This result is coherent with the CR hypothesis [10, 11] and results of past studies (e.g., [68]), where individuals with higher CR cope with and tolerate more age-related brain changes/pathologies and maintain better cognitive performance than those with lower CR. Hence, a higher CR may no longer facilitate cognitive performance when dementia-related neuropathology exceeds a certain critical threshold [69], albeit at a higher level than in individuals with lower/moderate CR. In individuals with larger brain volume, CR may not be as necessary to support cognitive performance since they are likely to show lower level of dementia-related neuropathology compared to those with more pronounced atrophy.

Sex and gender impacts on cognitive reserve and performance

Our results are similar to those of Bloomberg et al. [35] who report that women in all birth cohorts (1930 to 1938, 1939–1945, 1946–1955) outperformed men in verbal episodic memory (i.e., immediate recall of a word list) and language and semantic memory (i.e., semantic verbal fluency – animal). This finding is coherent with those of a recent meta-analysis showing an advantage for women on more verbal task in episodic memory [70]. However, previous studies of sex differences in semantic verbal fluency performance have yielded conflicting results, with some showing an advantage for men [71] or women [72]. This may be partly explained by the nature of specific semantic categories used in the verbal fluency test [72]. Furthermore, our results are in line with the recent finding showing that the Flynn effect (i.e., the observed rise over time in standardized intelligence test scores) is larger for women than for men [73], suggesting that women benefit more than men from improved living conditions [70]. Indeed, significant changes in gender roles have marked the last century, including increasing women's access to education and participation in the labor market [74]. In our sample, we showed that women who were born more recently had greater CR and held more complex jobs than their earlier-born counterparts, revealing gender improvements throughout the century. Regarding the increase in occupational complexity, women born during the earliest cohort (1915 to 1928) likely entered the labor force during the Great Depression (1929–1938), during which the highest unemployment rates were reached in the United States, while women born during the Great Depression likely entered the labor force during World War II (1939–1945), a pivotal period during

which women began to work in clerical jobs previously held by men in order to free them up to go to war. Women were employed in the United States historically, but married working women were mostly uneducated and worked in low-complexity jobs prior to the 1940s. They occupied the role of secondary workers in the family and their usefulness in the labor market faded when family incomes increased sufficiently [74]. Furthermore, regardless of sex or gender, a growing number of studies have shown that more challenging work environments, suggesting more complex occupations, are related to higher levels of cognitive functioning [75, 76]. Work environments that have complex demands and allow workers to exercise greater control and responsibility in decision-making are thought to promote cognitive functioning in adults [77]. Moreover, data from the Seattle Longitudinal Study suggest that later-born cohorts report exercising more control and innovation in their daily work lives [78].

Historical changes, cognitive reserve, and health

Over the past century and even more so during the first half of the 20th century, major historical events such as World Wars, pandemic and economic crisis, have caused our societies to evolve towards sociocultural changes that have influenced individual development [79]. Drastic changes are usually related to war and historical events, resulting in extremely unfavorable living conditions, interruption of education, and lack of health and social care in the early life. From 1910 to 1940, secondary schooling and graduation rates increased substantially in most of the United States, with the median years of school attained by the adult population, 25 years old and over, increasing from 8.1 to 8.6 years, and reaching 12.3 years during the 1940s and 1950s [80]. This rise in educational attainment may have enabled higher levels of complexity in occupational attainment [81] and promoted higher intellectual capacities [23]. Our results are coherent with these secular trends where proxies of CR improved across birth cohorts, with more recent-born participants having more education, more complex jobs, and higher verbal IQ at older ages, and thus higher CR, compared to their earlier-born counterparts. Previous studies showed similar increase of education level with successive birth cohorts (e.g., [30, 33, 82, 83]). Secular trends in proxies of CR can be considered as potential reasons for the improvement in cognitive performance across generations [34], which could offer the later-born participants an initial advantage in cognitive performance [32].

Likewise, increased accessibility to health care and advances in public health interventions (e.g., vaccinations) has contributed to reduced disease burden and improved living conditions [79]. Therefore, secular trends in vascular risk factors for dementia can also be investigated as potential explanations for the favorable trends in cognitive performances and dementia incidence [20, 21]. Based on data from five consecutive cross-sectional national surveys (1960 to 1998) among the United States population aged 20 to 74 years, the prevalence of hypertension and smoking has declined [84], and the prevalence of type 2 diabetes [85], hypercholesterolemia [84], and obesity [86] has increased. Coherent with this secular trend, we observed a significant decrease in rates of hypertension diagnosis, and an increase rate of obesity. Although not statistically significant, a downward trend in type 2 diabetes and smoking was observed across successive birth cohorts. Regarding the vascular index, the latter did not contribute significantly to any predictive model. Related to this reduction in vascular risk factor burden, we observed an improvement of structural brain health across birth cohorts, indicated by an increase of total brain volume and a decreased of total WMH volume. Although age could partly explain our result, a Rotterdam study reported a similar improvement in brain health in individuals aged 60 to 90 years—as indicated by larger brain volume, less brain atrophy and less cerebral small vessel disease—in the most recent cohort [87].

Strengths and limitations

One of the strengths of this study is the used of the ADNI data. This allows us to compare older adults aged 55 to 90 years, born up to 49 years apart, on the same cognitive tests and to study in more detail the structural brain health and vascular risk factors' burden. The birth cohorts were formed on the basis of major historical events that marked the past century and thus provide a better insight into the differences obtained. Furthermore, we considered multiple proxies of CR, allowing a more adequate estimation of CR. Limitations of this study include those related to the ADNI data. As such, assessment of sex is not exhaustive, as it is only observed (male or female), and gender was not evaluated. As the ADNI data is known for its educated and predominantly white participants; people who are socially disadvantaged are less likely to take part in such research [20], which

could limit the generalizability of our results. Further studies should clarify whether our results can be replicated with lower socioeconomic individuals. Because of the selection bias of highly educated participants, we further acknowledge that the somewhat restricted variability of the education level might not enable us to fully capture its statistical independent contribution. Also, birth cohort differences may be related to a selective survival bias with earlier born cohorts more likely to represent a more selected group of individuals. Likewise, our later born cohorts are younger than their earlier counterparts, which may have influenced the results.

CONCLUSIONS

To conclude, our study provides additional findings to the growing evidence of cohort differences in levels of cognitive performance favoring more recent birth cohorts and suggests that this association may be explained by the sociocultural improvements in proxies of CR. Our results revealed that later-born participants were more educated, held more complex jobs, and had higher verbal IQs than their earlier-born counterparts, which may have provided them an initial advantage in cognitive performance. The observations of larger birth cohort effects remain important for researchers and clinicians who use cognitive measures to assess cognitive functioning in older adults. Standardization of cognitive batteries, interpretation of test scores, establishment of cut-off scores, and decision-making based on cognitive assessments need to be done in the context of secular changes, that is cohort and generations effects [29].

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SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: http://dx.doi.org/10.3233/JAD-215044.

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