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Terminal Decline of Episodic Memory and Perceptual Speed in a Biracial Population

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Abstract

We compared trajectories of terminal cognitive decline in older Black (n= 3,372) and White (n=1,756) persons from a defined population who completed tests of episodic memory and perceptual speed at 3-year intervals for up to 18 years. During a mean of 9.9 years of observation, 1,608 Black persons and 902 White persons died. Preterminal decline of episodic memory did not differ by race. Terminal episodic memory decline began earlier in Black persons (mean of 4.3 years before death) than White persons (mean=3.9 years) and progressed more slowly. By contrast, terminal decline of perceptual speed began earlier in White persons (mean=5.0 years) than Black persons (mean=4.5 years). Rate of perceptual speed decline was more rapid in White persons than Black persons in both the preterminal and terminal periods. The results indicate that terminal cognitive decline occurs in Black persons but suggest that the rate of cognitive decline during the terminal period is less rapid in Black persons than White persons.

Keywords

terminal decline; longitudinal study; racial differences; episodic memory; perceptual speed

Introduction

The aging of the U.S. population has underscored the need to better understand the factors influencing the cognitive health of older persons. Because the elderly population is projected to become increasingly diverse in the next few decades, it is also important to determine whether the factors affecting cognition vary across racial or ethnic subgroups.

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Much of late-life cognitive decline is more strongly associated with impending mortality than advancing age. That is, many older persons experience little or no decline until the last few years of life when cognition declines rapidly for a variable period lasting about 3 to 8 years in most studies (Wilson, Beckett, Bienias, Evans, & Bennett, 2003; Sliwinski et al., 2006; Laukka, MacDonald, & Backman, 2006; Thorvaldsson et al., 2008; Muniz-Terrera et al., 2011; Wilson, Segawa, Hizel, Boyle, & Bennett, 2012; Muniz-Terrera et al., 2013). Dementia related pathologies such as neurofibrillary tangles and Lewy bodies are related to cognitive decline during the last few years of life, but substantial terminal cognitive decline is evident after controlling for common neurodegenerative and cerebrovascular pathologies (Wilson, Leurgans, Boyle, Schneider, & Bennett, 2010; Boyle et al., 2013; Wilson, Capuano, Bennett, Schneider, & Boyle, 2016). This supports the idea that mortality related factors have an association with late-life cognitive functioning that is at least partly independent of the pathologic processes traditionally linked to mild cognitive impairment and dementia in old age.

Although several longitudinal studies have compared trajectories of cognitive aging in older Black and White persons (Sloan & Wang, 2006; Karlamangla et al., 2009; Marsiske et al., 2013; Castora-Binkley, Peronto, Edwards, & Small, 2013; Early et al., 2013; Wilson, Capuano, Sytsma, Bennett, & Barnes, 2015), current knowledge about terminal changes in cognitive function is based almost entirely on research with White persons. Given the strong association between impending death and cognition, this represents a substantial gap in our understanding of late-life cognitive health in racial and ethnic minorities.

In the present study, we examined terminal changes in cognitive function in older Black and White residents of a geographically defined urban community. At 3-year intervals for up to 18 years, the study participants completed brief cognitive performance tests. Because previous research has suggested variability in trajectories of terminal decline across domains of cognition (Thorvaldsson et al., 2008; Batterham, Mackinnon, & Christensen, 2011; Wilson, Segawa, et al., 2012), analyses were based on previously established measures of episodic memory and perceptual speed. We used mixed-effects change point models to identify the onset of the terminal period and rate of cognitive change preceding and during the terminal period in each individual and to test for racial differences in these parameters.

Methods

Participants

Analyses are based on persons participating in the Chicago Health and Aging Project, a longitudinal population-based cohort study (Bienias, Beckett, Bennett, Wilson, & Evans, 2003). A geographically defined region in Chicago was censused from October 1993 to April 1997 and persons over the age of 65 were invited to participate in an in-home interview that included assessment of cognitive function. The interview was repeated at approximately 3-year intervals for 18 years.

Because analyses focused on nonlinear change in cognitive function, eligibility was restricted to those who had completed at least 3 triennial cognitive assessments. Of 10,802 study participants, 5,128 completed at least 3 interviews and analyses are based on this group. In comparison to the 5,674 who were ineligible, the eligible group included more Black persons (65.8% vs 60.6%, χ^2 [1]=30.6, p<0.001) and women (63.2% vs 60.0%, χ^2 [1]=12.1, p<0.001), and they were younger at baseline (71.4 vs 75.1, t[10,0340=28.9, p<0.001) and had higher levels of education, (12.5 vs 12.1, t[10,730=7.2, p<0.001), income (χ^2 [2]=15.6, p<0.001), and global cognitive function (as assessed by the Mini-Mental State Examination: 27.1 vs 25.1, χ^2 [1]=295.9, p<0.001). The ineligible group included 2,624 persons who completed 2 interviews. This ineligible subgroup had a similar percentage of women as the eligible group (61.5 vs 63.2, χ^2 [1] = 2.3, p=0.131) but fewer Black persons (61.3 vs 65.7, χ^2 [1] = 14.5, p<0.001) and lower level of education (12.2 vs 12.5, t[7,740] = 3.2, p=0.0014), higher level of income (χ^2 [1] = 10.1, p=0.007), and lower Mini-Mental State Examination score (26.1 vs 27.1, (χ^2 [1] = 59.9, p<0.001).

Assessment of Cognitive Function

As part of each triennial interview, cognitive function was assessed with 4 brief performance tests. The Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975) was used to measure global cognition. Because of its skewed distribution, it was used for descriptive purposes but not in longitudinal analyses. Episodic memory was assessed with immediate and delayed (after approximately 3 minutes) recall of 12 ideas contained in the East Boston Story (Albert et al., 1991; Wilson et al., 2002). Perceptual speed, a component of executive function, was assessed with a modified version (Wilson et al., 2002) of the oral form of the Symbol Digit Modalities Test (Smith, 1982). A composite measure of episodic memory was constructed by converting immediate and delayed recall raw scores to z scores, using the baseline mean and standard deviation in the entire population, and then averaging the z scores, as previously described (Wilson, Hebert, et al., 2012; Wilson et al., 2014). The raw score on the Symbol Digit Modalities Test was also converted to a z score to make it more comparable to the composite measure of episodic memory. Further information on these tests and their use in assessing late-life cognitive change is published elsewhere (Wilson et al., 1999; Wilson, Hebert, et al., 2012; Wilson et al., 2014).

Ascertainment of Vital Status

Information about all-cause mortality was collected from several sources. Study staff often learned of a participant's death and its date when attempting to schedule a follow-up interview. Staff also regularly scan area newspapers for obituaries and check websites such as www.ancestery.com. In addition, study personnel try to verify all deaths by acquiring death records from the National Death Index.

Statistical Analysis

Descriptive statistics were computed using means and standard deviations for continuous variables and percentages for categorical variables, and were stratified by race and death. We used a generalized linear model to test for differences in continuous and categorical measures with an indicator for race, an indicator for death, and a term for the interaction of race and death for the differential association of race with death.

To estimate the person-specific timing of change points in the cognitive measures before death, we used a Bayesian Monte Carlo Markov Chain approach (Gelman, Carlin, Stern, &

Rubin, 2003) with a single change point that allowed the rate of cognitive decline to accelerate after the change point and before death (Hall et al., 2001). These models used years before death as the time metric and provided estimates of 4 cognitive trajectory components: annual preterminal rate of cognitive change, change point, annual rate of terminal cognitive change, and level of cognition proximate to death. In addition, we used these 4 parameters to estimate the person-specific initial level of function in decedents, as previously described (Rajan et al., 2017).

For the Bayesian model, outcome measures were assumed to come from a normal distribution with the expected mean based on a linear function of fixed and random effects and unknown variance functions. The prior distribution for the inverse of the variance function was assumed to be from a gamma distribution with uninformative prior values. The person-specific intercepts, slopes, and change points were assumed to be from a multivariate normal distribution with hyperparameters for the inverse of the variance covariance matrix from a Wishart distribution. Two sets of initial values were used for the chains to estimate the mean and variance parameters to ensure convergence after the burning of the first 1000 observations and thinning of every 10 observations.

In survivors, there was little decline evident on inspection of the raw data and little support for a change point in preliminary analyses. Therefore, in a separate linear mixed model with random coefficients for intercept and slope, we estimated the level of baseline cognition and annual change in cognition function among survivors, using years from baseline as the time metric.

Given the 3-year interval between cognitive assessments, we imputed annual cognitive function test scores using the change between two consecutive observed assessments from a Gaussian distribution with the mean centered on this estimated annual score and random variation based on the differences observed in the population estimates during those data collection periods. By decreasing the temporal interval between outcomes, the imputation enhanced the convergence of the change point model. Because there has been little prior research on racial differences in terminal cognitive decline, we opted to construct separate models for Black and White participants. The models included random effects for the intercept, slopes, and change point as well as fixed effects for age and education. The outcome of the initial analyses was a measure of episodic memory. Analyses were then repeated with a measure of perceptual speed. The models were implemented in Open Bugs software (Lunn, Spiegelhalter, Thomas, & Best, 2009). We repeated each model twice, first including the 2,624 individuals who had completed 2 interviews and second in the primary analytic group but adding a time varying indicator for time to death.

Results

Table 1 shows the mean and standard deviation of each cognitive outcome measure at each wave of data collection in the 5,128 eligible participants. During a mean of 9.9 years of follow-up (SD=3.5), there were 2,510 deaths, including 1608 Black persons and 902 White persons (Table 2). At baseline, Black persons were younger than White persons and had lower levels of education and cognitive function. Mortality was related to older age at baseline and this association was stronger for White persons than Black persons. Mortality was also related to lower levels of education and cognition and these associations were marginally stronger for Black persons than White persons. Survivors had slightly more follow-up than decedents, but there were no racial differences in this regard.

Terminal Decline of Episodic Memory

To characterize change in the composite measure of episodic memory, we constructed a mixed-effects model that allowed rate of decline to accelerate at some variable point in the subgroup that died (Table 3). Among survivors, White persons had a higher baseline level of episodic memory function than Black persons, as shown by the estimate of the intercepts in Table 3. Rate of memory decline was modest in both Black and White survivors with a marginally slower rate in White survivors compared to Black survivors.

Those who died had a lower initial level of memory function than survivors. Rate of preterminal memory decline was similar in Black and White persons. At a mean of 4.32 years before death, there was a nearly tenfold increase in the mean rate of memory decline in the Black subgroup. Terminal memory decline in the White subgroup began slightly later (mean of 3.88 years before death) and proceeded at a slightly more rapid rate. Table 4 shows the model estimates of the correlations among cognitive trajectory components in deceased Black and White persons.

Figure 1 shows that there was considerable variability in the onset and rate of terminal episodic memory decline with approximately normal distributions of these parameters in each racial group. However, as shown in Figure 2, terminal decline in episodic memory in a typical Black participant (green dashed line) began nearly one half of a year earlier than in a typical White participant (blue dashed line) and progressed less rapidly.

Terminal Decline of Perceptual Speed

We constructed an identical change point model to characterize change in perceptual speed (Table 5). White survivors had a higher initial level of perceptual speed than Black survivors, but there were no racial differences in perceptual speed decline among survivors.

Among those who died, the initial level of perceptual speed was higher in White persons than Black persons. Preterminal decline in perceptual speed was slightly more rapid in White persons than Black persons. As shown in Figure 3, the onset and rate of terminal decline in perceptual speed were approximately normally distributed in each racial group. Terminal decline in perceptual speed began earlier and progressed more rapidly in White persons compared to Black persons.

As shown in the right side of Figure 2, terminal decline in perceptual speed began more than one half of a year later in a typical Black participant (green dashed line) than a typical White participant (blue dashed line). Figure 2 also shows that terminal decline in perceptual speed was much less precipitous in Black persons than White persons. Table 4 shows the correlations among cognitive trajectory components in deceased persons from each racial group.

Sensitivity Analyses

We excluded 2,624 individuals who had completed 2 interviews. To evaluate the impact of these exclusions, we repeated analyses with this subgroup included. As shown in Supplemental Tables 1 and 2, the results of these analyses were similar to the results of the original analyses (Tables 3 and 5).

To account for within person changes as individuals got closer to death, we added an indicator for distance to death (Piccinin, Muniz, Matthews, & Johannsson, 2011). These analyses (Supplemental Tables 3 and 4) were also comparable to the original models (Tables 3 and 5).

Discussion

We assessed episodic memory and perceptual speed at 3-year intervals in more than 5,000 older Black and White residents of an urban community. After a mean of 9.9 years of follow-up, nearly half of the participants had died. Decline in each cognitive domain was gradual in each racial group until a mean of 3 to 5 years before death when the rate of decline in each domain increased more than 6-fold in each racial group. The findings demonstrate that terminal decline of cognitive function occurs in Black persons and accounts for much of late-life loss of cognition.

As previously noted, prior research on terminal decline in cognitive function has been primarily conducted on White persons. These studies have observed variability in the onset of terminal cognitive decline, with most suggesting a mean onset approximately 3 to 8 years before death (Wilson et al., 2003; Sliwinski et al., 2006; Wilson, Beck, Bienias, & Bennett, 2007; Thorvaldsson et al., 2008; Batterham et al., 2011). Consistent with this research, we found that rate of decline in 2 cognitive domains accelerated a mean of 3 to 5 years prior to death in White persons. The current results extend previous research by demonstrating a similar accelerated decline in multiple cognitive domains beginning about 4 to 5 years before death in older Black persons, suggesting that the phenomenon of terminal cognitive decline at least partly generalizes across racial groups.

Although there were racial differences in the onset of terminal decline, these differences were not consistent across cognitive domains. Thus, on average terminal decline of episodic memory began about half of a year earlier in Black persons than White persons whereas terminal decline of perceptual speed began about half of a year later in Black persons than White persons. In both cognitive domains, the rate of terminal decline was less rapid in Black persons than White persons. The racial differences in terminal decline of episodic memory were relatively small. However, the racial differences in terminal decline of perceptual speed were so large that the racial groups were performing at approximately the same level proximate to death despite a substantially higher baseline level of performance in the White group compared to the Black group.

Why terminal cognitive decline was slower in Black persons than White persons in uncertain. It is possible that pre-existing racial differences in level of cognitive function contributed to the finding. Model estimates of initial level of function (i.e., intercept) were correlated with estimates of the rate of terminal cognitive decline in both Black and White persons (Table 4). However, these correlations were stronger in White persons than Black persons, and there were not clear racial differences in rates of preterminal cognitive change despite robust correlations between the intercept and preterminal rate of change in both Black and White persons, making this explanation less likely. Another possibility is that floor artifacts limited our ability to assess rapid rates of terminal decline in the Black subgroup, but Figures 1 and 3 do not suggest racial differences in the distribution of estimated slopes during the terminal period. Further research on terminal cognitive decline in racial and ethnic minorities is needed.

In both racial groups, the mean onset of terminal decline of perceptual speed preceded the mean onset of terminal decline in episodic memory. This observation is consistent with two previous studies of predominantly White persons (Batterham et al., 2011; Wilson, Segawa, et al., 2012). It suggests that perceptual speed and perhaps other components of executive functioning are especially sensitive to the changes in the brain underlying terminal cognitive decline. In this cohort, Black persons experienced less preterminal decline in perceptual speed than White persons, which is consistent with previous cognitive aging studies (Early et al., 2013; Wilson, Capuano, Sytsma, Bennett & Barnes, 2015). This suggests that Black persons may have begun the terminal period with a relatively healthier perceptual speed system which provided some protection against the changes in the brain driving terminal cognitive decline. It is noteworthy that higher level of conscientiousness is also associated with better executive functioning (Ackerman & Heggestad, 1997; Booth, Schinka, Brown, Mortimer, & Borenstein, 2006; Wilson, Schneider, Arnold, Bienias, & Bennett, 2007) and with reduced terminal cognitive decline (Wilson, Boyle, et al., 2015). This suggests that individual differences in preterminal brain structure and function influence how terminal changes in the brain are behaviorally expressed.

The present study has notable strengths and limitations. Analyses are based on a large group of older persons sampled from a geographically defined area, making it more likely that the racial subgroups are comparable. In addition, multiple cognitive domains were assessed at regular intervals for a mean of nearly 10 years, enhancing our ability to reliably characterize nonlinear trajectories of cognitive decline. The primary limitation is that the interval of 3 years between cognitive assessments is relatively long which may have affected the accuracy of the estimates of terminal decline onset though the use of imputed annual scores may have lessened this problem. The time metric was years before death in the deceased and years from baseline in survivors, but we have previously shown that these metrics yield equivalent estimates of rate of cognitive change (Boyle et al., 2013).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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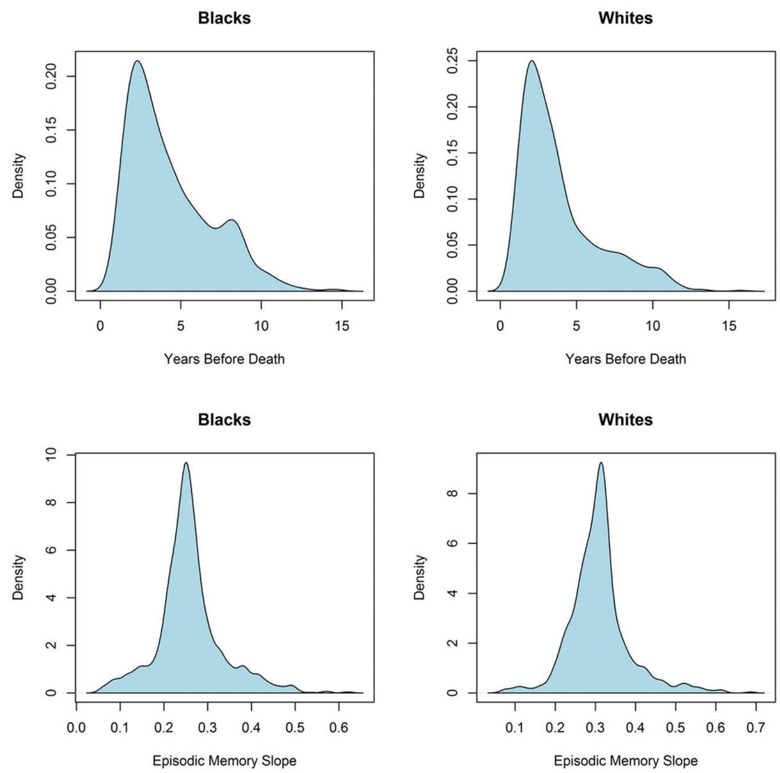

Figure 1.

Distributions of the person-specific onsets (upper histograms) and slopes (lower histograms) of terminal decline in episodic memory in Black (histograms on left) and White (histograms on right) persons, from mixed-effects change point models adjusted for age and education.

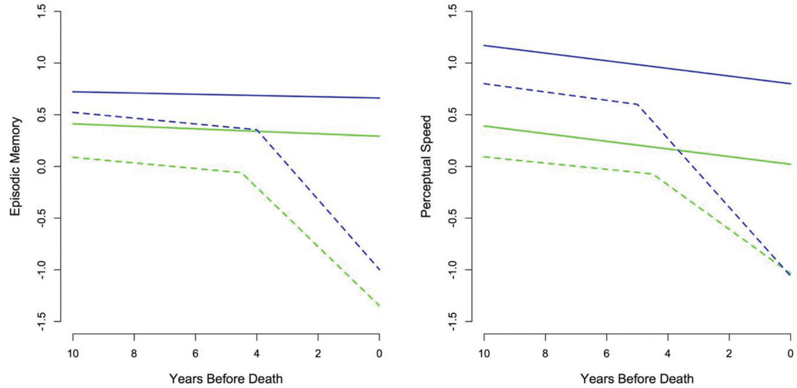

Figure 2.
Person-specific 10-year trajectories of change in episodic memory (left) and perceptual speed (right) in typical Black (green line) and White (blue line) participants who survived (solid line) or died after 10 years of observation (dashed line), from mixed-effects change point models adjusted for age and education.

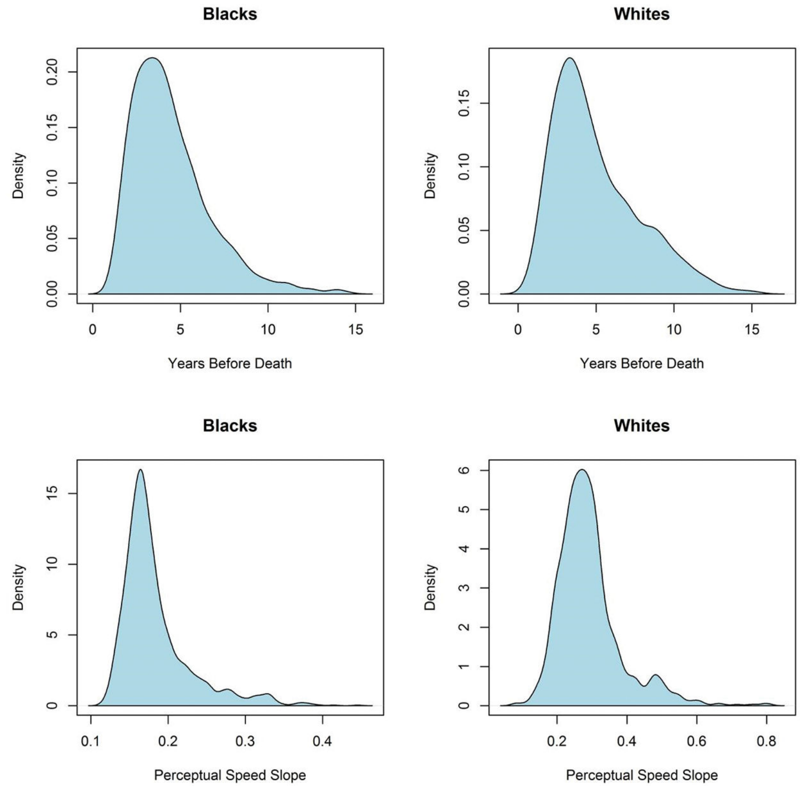

Figure 3.

Distributions of the person-specific onsets (upper histograms) and slopes (lower histograms) of terminal decline in perceptual speed in Black (histograms on left) and White (histograms on right) persons, from mixed-effects change point models adjusted for age and education.

Table 1

Episodic memory and perceptual speed scores at each triennial interview

		Decedents			Survivors		
Interview wave	Cognitive outcome	No. participants	Mean	SD	No. participants	Mean	SD
1	Episodic memory	2496	0.168	0.824	2601	0.500	0.690
	Perceptual speed	2458	0.156	0.922	2598	0.660	0.842
2	Episodic memory	2442	0.026	0.909	2535	0.470	0.719
	Perceptual speed	2318	0.046	0.881	2526	0.568	0.862
3	Episodic memory	2309	−0.065	1.088	2410	0.481	0.718
	Perceptual speed	2154	−0.121	0.948	2395	0.484	0.846
4	Episodic memory	1501	−0.132	1.146	1642	0.405	0.784
	Perceptual speed	1427	−0.295	0.996	1630	0.291	0.961
5	Episodic memory	666	−0.135	1.158	770	0.400	0.867
	Perceptual speed	638	−0.345	0.925	768	0.272	0.823
6	Episodic memory	301	−0.483	1.206	714	0.177	0.926
	Perceptual speed	275	−0.508	0.902	711	0.017	0.866

Table 2

Descriptive information on participants who survived and those who died

	Survived (n=2,618)		Died (n=2,510)		p-Value		
Characteristic	**Black (n=1,761)**	**White (n=857)**	**Black (n=1,608)**	**White (n=902)**	**Race**	**Death**	**Race × Death**
Age at baseline	68.8 (3.2)	70.2 (4.6)	72.5 (5.5)	75.4 (6.4)	<.0001	<.0001	<.0001
Years of education	12.2 (3.2)	14.6 (3.1)	10.9 (3.4)	13.8 (3.4)	<.0001	<.0001	0.0104
Women, n%	1179 (68.6)	539 (31.4)	958 (62.9)	566 (37.1)	0.0638	0.8734	0.0151
MMSE score at baseline	27.4 (2.7)	28.9 (1.3)	25.5 (4.5)	28.0 (2.5)	<.0001	<.0001	<.0001
Memory score at baseline	0.4 (0.7)	0.7 (0.6)	0.0 (0.9)	0.4 (0.7)	<.0001	<.0001	0.0625
Speed score at baseline	0.4 (0.8)	1.2 (0.6)	−0.2 (0.9)	0.7 (0.7)	<.0001	<.0001	0.0179
Years of follow-up	10.3 (3.6)	10.2 (4.0)	9.6 (3.2)	9.6 (3.3)	0.5739	0.0014	0.4195

Note. Data are presented as mean (standard deviation) unless otherwise indicated. P values are based on generalized linear models.

Table 3

Change in episodic memory in Black and White persons

		Survived		Died	
Racial subgroup	**Model Term**	**Coefficient**	**95% CI**	**Coefficient**	**95% CI**
Black persons	Intercept	0.412	0.382, 0.441	0.088	0.022, 0.158
	Preterminal time	0.012	0.003, 0.021	0.027	0.024, 0.029
	Change point			4.32	4.05, 4.56
	Terminal Time			0.259	0.241, 0.275
White Persons	Intercept	0.722	0.690, 0.754	0.523	0.423, 0.613
	Preterminal Time	0.006	0.002, 0.011	0.028	0.025, 0.030
	Change point			3.88	3.84, 4.13
	Terminal time			0.310	0.287, 0.333

Note. From mixed-effects change point models adjusted for age and education. CI, credible interval.

Table 4

Correlations between cognitive trajectory components in Black and White persons

Cognitive outcome	Trajectory components	Black persons Correlation	White persons Correlation
Episodic memory	intercept, preterminal slope	.73	.71
	intercept, change point	.96	.95
	intercept, terminal slope	.18	.43
	preterminal slope, change point	.83	.81
	preterminal slope, terminal slope	.22	.09
	change point, terminal slope	.15	.20
Perceptual speed	intercept, preterminal slope	.47	.58
	intercept, change point	.70	.82
	intercept, terminal slope	.37	.59
	preterminal slope, change point	.79	.66
	preterminal slope, terminal slope	.46	.18
	change point, terminal slope	.68	.18

Note. From mixed-effects change point models adjusted for age and education. All $p<.01$.

Table 5

Change in perceptual speed in Black and White persons

		Survived		Died	
Racial subgroup	**Model Term**	**Coefficient**	**95% CI**	**Coefficient**	**95% CI**
Black persons	Intercept	0.391	0.356, 0.426	0.147	0.092, 0.201
	Preterminal time	0.037	0.034, 0.041	0.030	0.027, 0.032
	Change point			4.46	4.19, 4.74
	Terminal Time			0.184	0.171, 0.199
White Persons	Intercept	1.170	1.128, 1.211	0.800	0.709, 0.890
	Preterminal Time	0.037	0.032, 0.041	0.040	0.037, 0.043
	Change point			5.00	4.69, 5.30
	Terminal time			0.292	0.273, 0.311

Note. From mixed-effects change point models adjusted for age and education. CI, credible interval.