

Cognition and survival in a biracial urban population of old people

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ABSTRACT

We examined the relation of level of cognition to survival in a biracial community population of more than 10,000 older persons. At baseline, participants completed 4 cognitive tests from which a composite global cognitive measure was derived. During up to 14 years of follow-up (mean = 6.9 years), 4201 people died (41.6%). Higher level of cognitive function was associated with increased survival even after controlling for health related and lifestyle variables. The association did not differ between African Americans and whites; it was stronger in older than younger persons; and it was especially pronounced for perceptual speed. The results underscore the importance of cognition to survival in old age.

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In population-based studies of old people, better cognitive function, whether measured psychometrically (Arauz et al., 2005; Anstey, Luszcz, Giles, & Andrews, 2001; Gale, Martyn, & Cooper, 1996; Kelman, Thomas, Kennedy, & Cheng, 1994; Liu, LaCroix, White, Kittner, & Wolf, 1990; Maier & Smith, 1999; Portin et al., 2001; Small & Backman, 1997; Smits, Deeg, Kriegsman, & Schmand, 1999) or by diagnostic categories (Katzman et al., 1994; Evans et al., 1991; Hebert, Scherr, McCann, Beckett, & Evans, 2001; Aguero-Torres, Fratiglioni, Guo, Viitanen, & Winblad, 1999; Helmer, Joly, Letenneur, Commenges, & Dartigues, 2001; Tschanz et al., 2004), has been associated with increased survival, and cognitive impairment has been identified as a leading cause of death (Borjesson-Hanson, Gustafson, & Skoog, 2007; Hoyert & Rosenberg, 1997; Tschanz et al., 2004). Despite this volume of evidence, there are several gaps in current knowledge. For example, most research is based on white or Hispanic persons. So information about the relation of cognition to survival in older African Americans is

sparse. Because cognition tends to decline in old people who are about to die (Thorvaldsson et al., 2008), the association of cognition with death should strengthen with advancing age, but few data on this point are available. The extent to which health and behavioral variables are contributing to the association is not well understood (Sabia et al., *in press*). Finally, although all forms of cognition appear to be related to mortality, some studies suggest that the correlation varies across domains of cognitive function (Small & Backman, 1997; White & Cunningham, 1988; Portin et al., 2001; Bosworth, Schaie, & Willis, 1999; Johnson, Liu, & Yaffe, 2007). There is no consensus on which cognitive domain is most strongly associated with mortality, however.

In this article, we examine the relation of cognition to survival in more than 10,000 older African Americans and whites residing in a geographically defined community in Chicago. Cognition was assessed at baseline with brief measures of episodic memory, perceptual speed, and global cognition, and vital status was monitored up to 14 years (mean = 6.9 years). In a series of proportional hazards models, we first estimated the association between cognition and risk of death using a composite measure of global cognition based on all measures. We then tested for racial and age differences, examined health

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related and lifestyle variables that might account for the association, and assessed the correlation using the individual cognitive tests.

1. Methods

1.1. Participants

Subjects are from the Chicago Health and Aging Project, a longitudinal study of aging and Alzheimer's disease conducted in three adjacent neighborhoods in Chicago. The project is described in detail elsewhere (Bienias, Beckett, Bennett, Wilson, & Evans, 2003; Morris et al., 2002; Wilson et al., 2005). Following a census of the community from October 1993 to April 1997, persons over the age of 65 were invited to participate in an in home interview. The interview was repeated at intervals of approximately 3 years, and residents who had become 65 since the previous population interview were added to the cohort. At the time of these analyses, 10,121 persons had completed the baseline interview. They had a mean age of 73.3 (SD = 7.1), a mean of 12.2 years of formal education (SD = 3.6), and a mean score of 25.9 on the Mini-Mental State Examination (SD = 5.3); 60.9% were women and 64.4% were African American.

1.2. Assessment of cognitive function

Four brief cognitive performance tests were administered as part of the in home interview: immediate and delayed recall of 12 ideas contained in the East Boston Story (Albert, Smith, Scherr, Taylor, & Evans, 1991; Wilson, Beckett et al., 2002); the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975), a widely used 30-item mental status test; and a modified form of the oral version of the Symbol Digit Modalities Test (Smith, 1982), a symbol substitution procedure that assesses perceptual speed. Because the tests loaded on a single factor that accounted for approximately 75% of the variance in a previous factor analysis (Wilson et al., 1999), we constructed a composite measure of global cognition based on all 4 tests. As previously described, raw scores on each test were converted to *z* scores, using the population mean and standard deviation, and the *z* scores were averaged to yield the composite measure (Wilson et al., 1999; Wilson et al., 2005).

1.3. Assessment of vital status

Data about all-cause mortality were ascertained from multiple sources. When project personnel attempted to schedule follow-up interviews, done at 3-year intervals, they might be informed of a subject's death and its date by family members or friends. We also regularly scan local newspapers for obituaries, search web sites (e.g., www.Ancestry.com), and attempt to verify deaths by acquiring a death record from the National Death Index. For the deceased, the date of death was the censoring date; for survivors, it was 3/31/2008.

1.4. Assessment of covariates

Classification of five chronic medical conditions was as follows: heart disease was based on history of myocardial infarction or bypass graft surgery, angina pectoris, or use of digitalis; hypertension was based on history, measured blood

pressure > 160 mm Hg systolic or > 95 mm Hg diastolic; or use of antihypertensive medication; stroke, based on history; diabetes mellitus, based on history or use of insulin or oral hypoglycemic medication; and cancer, based on history. Weight divided by height squared (kg/m^2) was used as an index of body mass. Tobacco use was classified as current, former, or never.

We quantified baseline levels of cognitive activity, social engagement, and physical activity with previously established measures. Participants rated their frequency of participation in seven cognitively stimulating activities (e.g., reading a book) from 1 (once a year or less) to 5 (everyday or about everyday), as previously described (Wilson et al., 1999; Wilson, Bennett et al., 2002). Four questions about involvement in social activities (e.g., participation in activities or groups outside the home, part-time or full-time employment) were used to measure social engagement. Item scores were summed to yield a total score that ranged from 0 to 8, as previously described (Barnes, Mendes de Leon, Wilson, Bienias, & Evans, 2004; Wilson et al., 2005). Physical activity was assessed with questions adapted (McPhillips et al., 1989) from the 1985 Health Interview Survey (Moss & Parsons, 1986). Subjects indicated if they had participated in each of 9 activities (e.g., walking for exercise) in the last 2 weeks plus how often they had done so and for how long. Total hours per week spent in the 9 activities was used in analyses (Wilson, Bennett et al., 2002; Wilson et al., 2005).

We assessed depressive symptoms with the Center for Epidemiological Studies Depression Scale (Radloff, 1977), using a 10-item form shown to be psychometrically similar to the original (Kohout, Berkman, Evans, & Cornoni-Huntley, 1993). Participants indicated for each of ten symptoms whether they had felt that way much of the time in the last week. In prior research, the number of symptoms on this scale has been associated with risk of dementia (Wilson, Barnes et al., 2002) and death (Wilson, Bienias, Mendes de Leon, Evans, & Bennett, 2003).

1.5. Data analysis

We used proportional hazards models (Cox, 1972) to estimate the effect of a 1-point increase in cognitive test score on risk of death. All analyses included terms to control for age, sex, race, and education. The initial model included a term for global cognitive score at baseline. We then repeated the analysis with a term added for the interaction of race with global cognition; with a term added for the interaction of age with global cognition; with terms for health related variables; excluding persons who died soon after cognition was assessed; with a term added for depressive symptoms; with terms added for activity participation; and with all covariates in a single model. We then repeated a subset of these analyses using individual cognitive tests in place of the composite measure of global cognition. Programming was done in SAS (SAS Institute Inc., 2004).

2. Results

2.1. All-cause mortality

During up to 14 years of observation (mean = 6.9, SD = 4.4), 4206 persons died (41.6%). As shown in Table 1,

Table 1

Baseline characteristics of persons who survived or died during the study period.

Characteristic	Survived (<i>n</i> = 5915)	Died (<i>n</i> = 4206)	<i>p</i> -value
Age, year	70.9 (5.5)	76.5 (7.7)	<0.001
Education, year	12.7 (3.3)	11.4 (3.7)	<0.001
Women, %	63.6	57.2	<0.001
African American, %	64.8	61.5	<0.001
Global cognition	0.41 (0.62)	−0.23 (0.97)	<0.001
Mini-mental state exam.	27.4 (3.2)	23.9 (6.8)	<0.001
Symbol digit	33.1 (12.8)	22.4 (14.4)	<0.001
Imm. story recall	9.1 (2.4)	7.4 (3.2)	<0.001
Del. story recall	8.6 (2.6)	6.7 (3.5)	<0.001
Hypertension, %	58.1	55.1	0.002
Stroke, %	6.6	13.7	<0.001
Diabetes, %	17.8	21.3	<0.001
Heart disease, %	10.5	18.1	<0.001
Cancer, %	16.5	20.0	<0.001
Body mass index	28.8 (5.9)	26.2 (5.8)	<0.001
Current smoking, %	13.1	16.0	<0.001
Former smoking, %	38.4	40.2	0.056
Cognitive activity	3.24 (0.64)	2.91 (0.73)	<0.001
Social activity	2.60 (1.68)	1.93 (1.63)	<0.001
Physical activity	1.41 (1.26)	1.10 (1.13)	<0.001
Depressive symptoms	1.35 (1.86)	1.91 (2.20)	<0.001

Note. All data are mean (SD) unless otherwise indicated.

those who died were older and less educated than survivors and more apt to be male and white. They also had lower levels of cognitive function and lifestyle activity and more common chronic medical conditions and risk factors for mortality.

2.2. Cognitive function and survival

To make use of all cognitive data, we used the composite measure of global cognition in most analyses. It ranged from −4.31 to 1.73 (mean = 0.14, SD = 0.84), with higher scores indicating better cognitive function. We estimated the relation of baseline cognitive score to risk of death in a series of proportional hazards models that controlled for age, sex, race, and education. In the initial analysis, higher global cognitive score was associated with a decreased risk of death (hazard ratio [HR] = 0.59; 95% confidence interval [CI]: 0.57, 0.62). Fig. 1, which is based on this analysis, shows that the risk of death associated with a global cognitive score at the 75th percentile (score = 0.73) was reduced by about 62% relative to a score at the 25th percentile (score = −0.21), approximately equivalent to being 7 years younger (HR for age = 1.07; 95% CI: 1.07, 1.08).

Knowledge about the association of cognitive function with survival in African Americans is limited, and in a linear regression model adjusted for age, sex, and education, global cognitive performance was lower in black than white participant (estimate = −0.43, SE = 0.002, $p < 0.001$). Therefore, we repeated the original survival model with a term added for the interaction of global cognition by race. There was no interaction (estimate = 0.027, SE = 0.034, $p = 0.430$), indicating that the association of level of cognition with survival in black persons was similar to the association in white persons.

To see if age modified the relation of cognition to survival, we tested for an interaction between age and global cognitive score. There was an interaction (estimate = 0.011, SE = 0.002, $p < 0.001$) such that the association of cognition with survival was stronger in older than younger participants.

At the time of enrolling in the study, those who subsequently died had more chronic medical conditions and risk factors for mortality than survivors. To determine whether these health related variables could account for the association of cognition with survival, we repeated the analysis with terms for five medical conditions (i.e., hypertension, stroke, diabetes, heart disease, cancer), body mass index, and current and former cigarette smoking. In this model, the association of global cognition with survival (HR = 0.60; 95% CI: 0.57, 0.63; effect reduced by approximately 2%) was similar to the original analysis. The difference in mortality across the interquartile range of global cognition in this model, 60%, exceeded the risk associated with all of the medical and health-related variables in the analysis except for current smoking which increased risk of death by about 67% (HR = 1.67; 95% CI: 1.51, 1.85).

To further examine the impact of health on results, we repeated the original analysis after excluding individuals who died within one year of cognitive testing ($n = 479$). The relation of global cognitive score to survival (HR = 0.60; 95% CI: 0.57, 0.62) was similar to the original model. Results were comparable in subsequent analyses after excluding those who died within two ($n = 924$; HR = 0.59; 95% CI: 0.57, 0.62) or three ($n = 1296$; HR = 0.61; 95% CI: 0.58, 0.64) years of cognitive assessment.

Higher level of depressive symptoms is associated with mortality (Wilson, Bienias et al., 2003) and loss of cognition (Wilson, Barnes et al., 2002). Adjustment for number of depressive symptoms on the Center for Epidemiological Studies Depression Scale did not affect the correlation of global cognition with mortality, however (HR = 0.60; 95% CI: 0.58, 0.63).

Because frequency of cognitive, social, and physical activity has been related to both cognition (Wilson, Bennett et al., 2003; Barnes et al., 2004) and mortality (Wilson et al., 2005) in this population, we repeated the original analysis with terms for these variables. Global cognition continued to be associated with survival (HR = 0.65; 95% CI: 0.63, 0.68), but the effect was reduced by approximately 18% compared to the original analyses. Results were similar when all of the health, affect, and activity covariates were included in the same model (HR = 0.64; 95% CI: 0.61, 0.68).

To examine whether the association of cognition with survival varied across cognitive domains, we conducted separate analyses for each of the 4 individual cognitive tests

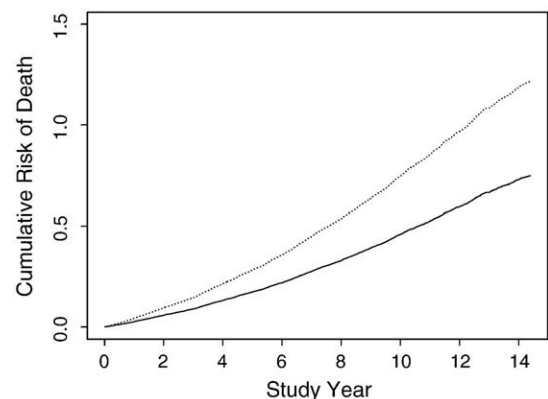


Fig. 1. Cumulative risk of death associated with a global cognitive score at the 25th (dotted line) and 75th (solid line) percentiles, adjusted for age, sex, race, and education.

Table 2
Relation of baseline cognitive score to survival.

Cognitive measure	Model A	Model B	Model C	Model D
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Mini-mental state examination	0.94 (0.93, 0.94)	0.94 (0.93, 0.95)	0.93 (0.93, 0.94)	0.95 (0.94, 0.95)
Symbol digit modalities test	0.97 (0.96, 0.97)	0.97 (0.97, 0.97)	0.97 (0.96, 0.97)	0.97 (0.97, 0.97)
Immediate story recall	0.91 (0.90, 0.92)	0.92 (0.91, 0.93)	0.92 (0.91, 0.93)	0.93 (0.92, 0.94)
Delayed story recall	0.92 (0.91, 0.93)	0.92 (0.91, 0.93)	0.92 (0.91, 0.93)	0.93 (0.92, 0.94)

Note. Results show the effect on survival of a 1-point increase in cognitive score estimated from separate proportional hazards models. All models controlled for age, sex, race, and education. In addition, model B controlled for health related variables, model C for depressive symptoms, and model D for lifestyle activities.

(model A, Table 2). In each case, higher cognitive score was related to increased survival. To access the relative size of these effects, we plotted the predicted cumulative risk of death associated with scores at the 25th and 75th percentiles on each test (Fig. 2). The difference in mortality risk across the interquartile ranges of the Mini-Mental State Examination and both story recall measures is about 30% compared to a difference of more than 100% for the Symbol Digit Modalities Test, equivalent to about 11 years of age. As shown in Table 2, results were similar after controlling for health related variables (model B), depressive symptoms (model C), or lifestyle activities (model D).

3. Discussion

We examined the relation of cognition in late life to survival in more than 10,000 older residents of an urban

community. During a mean of about 7 years of observation, more than 40% of the cohort died, and risk of death was about 60% greater in those with low average cognitive function compared to those with high average function. This finding is consistent with prior population research (Arauz et al., 2005; Anstey et al., 2001; Gale et al., 1996; Kelman et al., 1994; Liu et al., 1990; Maier & Smith, 1999; Portin et al., 2001; Small & Backman, 1997; Smits et al., 1999) and underscores the strong link between cognition and survival in old age.

Little is know about cognitive function and survival in African Americans. Despite differences between black and white residents in level of cognitive performance, the correlation of cognitive performance with mortality was equivalent in the two racial subgroups. Similar results have been reported in Hispanic cohorts (Arauz et al., 2005; Nguyen, Black, Ray, Espino, & Markides, 2003), suggesting that the association generalizes across racial and ethnic lines.

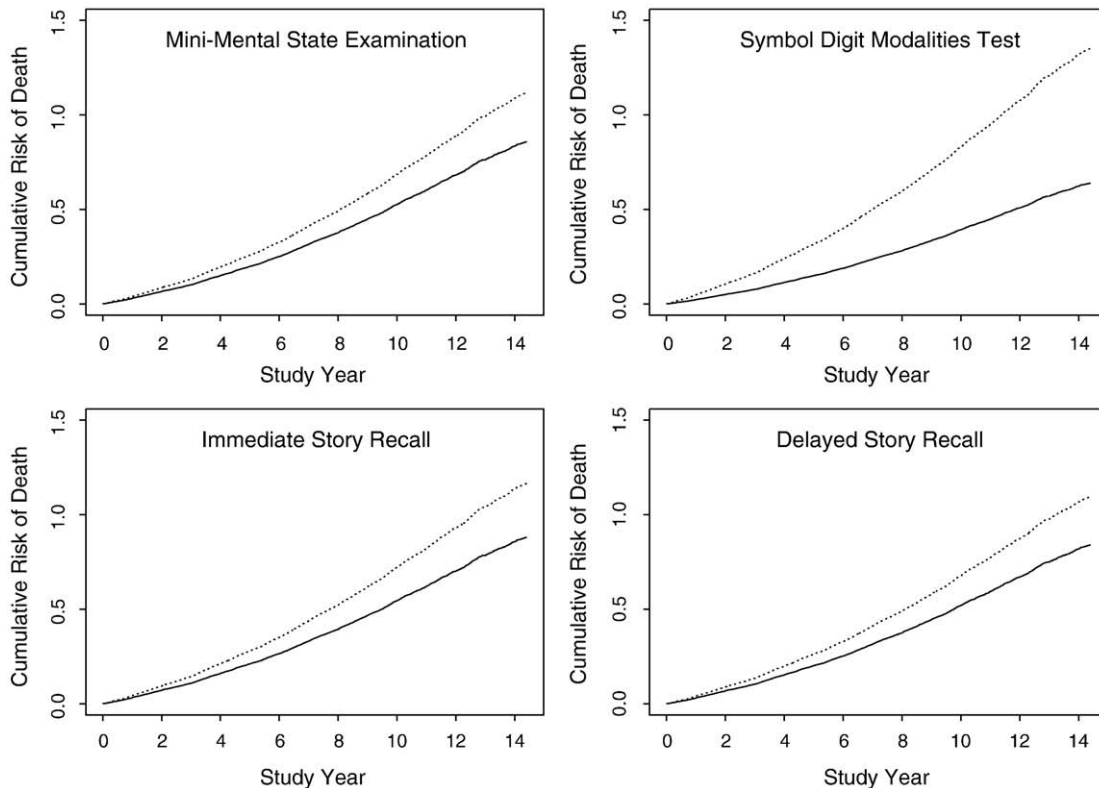


Fig. 2. Cumulative risk of death associated with cognitive scores at the 25th (dotted lines) and 75th (solid line) percentiles for the Mini-Mental State Examination, Symbol Digit Modalities Test and immediate and delayed story recall, adjusted for age, sex, race, and education.

It has been difficult to establish whether some cognitive functions are more strongly related to mortality than others. In this cohort, all cognitive measures were associated with mortality, suggestive of a more general effect, consistent with much previous research (Maier & Smith, 1999; Shipley, Der, Taylor, & Deary, 2007; Small, Fratiglioni, von Strauss, & Backman, 2003; Weatherbee & Allaire, 2008a,b). Other studies have suggested a more selective effect but with little consensus on the cognitive abilities most strongly related to mortality, with some studies suggesting verbal skills (Small & Backman, 1997; White & Cunningham, 1988) and others identifying episodic memory (Small & Backman, 1997; Portin et al., 2001) or perceptual speed/executive function (Bosworth et al., 1999; Fried et al., 1998; Johnson et al., 2007). The findings from this cohort agree with the latter studies: a measure of perceptual speed that draws upon executive functions had a substantially stronger association with mortality than did measures of global cognition or episodic memory. Executive function also appears to have a selective association with disability in old age (Grisby, Kay, Baxter, Shetterly, & Hammon, 1998; Cahn-Weiner, Malloy, Boyle, Marran, & Salloway, 2000). As neuropathologic changes occur and begin to impair cognitive, sensory, and motor functions, strong executive skills may help older individuals adapt and make the most of their remaining capabilities (Boyle, Wilson, Schneider, Bienias, & Bennett, 2008). These data suggest that interventions designed to enhance complex attentional skills (Jaeggi, Buschkuhl, Jonides, & Perrig, 2008) may benefit older persons.

The bases of the correlation between cognition and survival in old age are uncertain. Level of cognition in early life (Batty, Deary, & Gottfredson, 2007; Whalley & Deary, 2001) and middle age (Sabia et al., in press) also predicts mortality, demonstrating a survival advantage for higher cognitive function across the life span (Shipley, Der, Taylor, & Deary, 2006). A previous study of a middle-aged cohort found that the association was mediated in part by healthy behaviors (Sabia et al., in press). Consistent with this idea, the correlation of cognition with survival in this study was reduced by about one fifth after adjusting for level of cognitive, social, and physical activity. Thus, engagement in a healthier lifestyle may partially account for the association of higher cognition with increased survival. It is likely that the correlation of cognition with survival in old age also reflects factors other than health related behaviors. In this population, the correlation of cognition with survival was stronger in the old-old than in the young-old. This observation is consistent with longitudinal evidence that cognition declines at an accelerated pace in the last years of life (Sliwinski et al., 2006; Wilson, Beckett, Bienias, Evans, & Bennett, 2003; Wilson, Beck, Bienias, & Bennett, 2007). Because Alzheimer's disease pathologic changes are commonly found in the brains of old people who die without dementia and are inversely related to cognition in this subgroup (Bennett, Schneider, Wilson, Bienias, & Arnold, 2005; Bennett et al., 2006), these terminal changes in cognitive function are probably due in part to Alzheimer's disease.

This study has important strengths and limitations. Results are based on a geographically defined population of old people, minimizing selection bias and ensuring a broad spectrum of cognitive ability. That African Americans and whites were sampled from the same population enhanced our ability

to meaningfully compare racial subgroups, and the large size of the population increased our power to do so. Because of the heterogeneity in rates of change in cognitive function in old age, it is likely that our cross-sectional measures of cognition underestimate the true correlation between cognition and mortality in old age. Also, the somewhat crude measures of health related variables may have led us to underestimate their associations with mortality.

In summary, we found a robust linear association between cognitive ability, especially perceptual speed, and mortality. The association was similar for African Americans and whites and was comparable in size to effects observed from some common chronic medical conditions such as diabetes and heart disease. The results further demonstrate the malignant nature of cognitive impairment in old age.

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