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Cognitive Resilience to Apolipoprotein E ϵ 4:

Contributing Factors in Black and White Older Adults

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Abstract

IMPORTANCE—Apolipoprotein E (*APOE*) ϵ 4 is an established risk factor for cognitive decline and the development of dementia, but other factors may help to minimize its effects.

OBJECTIVE—Using *APOE* ϵ 4 as an indicator of high risk, we investigated factors associated with cognitive resilience among black and white older adults who are *APOE* ϵ 4 carriers.

DESIGN, SETTING, AND PARTICIPANTS—Participants included 2487 community-dwelling older (aged 69–80 years at baseline) black and white adults examined at 2 community clinics in the prospective cohort Health, Aging, and Body Composition (Health ABC) study. The baseline visits occurred from May 1997 through June 1998. Our primary analytic cohort consisted of 670 *APOE* ϵ 4 carriers (329 black and 341 white participants) who were free of cognitive impairment at

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Study concept and design: Kaup, Yaffe.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Kaup, Yaffe.

Critical revision of the manuscript for important intellectual content: All authors.

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Study supervision: Yaffe.

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baseline and underwent repeated cognitive testing during an 11-year follow-up (through 2008) using the Modified Mini-Mental State Examination.

MAIN OUTCOMES AND MEASURES—We stratified all analyses by race. Using the Modified Mini-Mental State Examination scores, we assessed normative cognitive change in the entire cohort ($n = 2487$) and classified the *APOE* $\epsilon 4$ carriers as being cognitively resilient vs nonresilient by comparing their cognitive trajectories with those of the entire cohort. We then conducted bivariate analyses and multivariable random forest and logistic regression analyses to explore factors predictive of cognitive resilience in *APOE* $\epsilon 4$ carriers.

RESULTS—Among white *APOE* $\epsilon 4$ carriers, the strongest predictors of cognitive resilience were, in relative order of importance, no recent negative life events, a higher literacy level, advanced age, a higher educational level, and more time spent reading. Among black *APOE* $\epsilon 4$ carriers, the strongest predictors of cognitive resilience were, in relative order of importance, a higher literacy level, a higher educational level, female sex, and the absence of diabetes mellitus. In follow-up logistic regression models, higher literacy level (adjusted odds ratio [OR], 9.50 [95% CI, 2.67–60.89]), a higher educational level (adjusted OR for college graduate vs less than high school, 3.81 [95% CI, 1.13–17.56]), and age (adjusted OR for 73–76 vs 69–72 years, 2.01 [95% CI, 1.13–3.63]) had significant independent effects in predicting cognitive resilience among white *APOE* $\epsilon 4$ carriers. Among black *APOE* $\epsilon 4$ carriers, a higher literacy level (adjusted OR, 2.27 [95% CI, 1.29–4.06]) and a higher educational level (adjusted OR for high school graduate/some college vs less than high school, 2.86 [95% CI, 1.54–5.49]; adjusted OR for college graduate vs less than high school, 2.52 [95% CI, 1.14–5.62]) had significant independent effects in predicting cognitive resilience.

CONCLUSIONS AND RELEVANCE—Although *APOE* $\epsilon 4$ carriers are at high risk for cognitive decline, our findings suggest possible intervention targets, including the enhancement of cognitive reserve and improvement of other psychosocial and health factors, to promote cognitive resilience among black and white *APOE* $\epsilon 4$ carriers.

Carriers of apolipoprotein E (*APOE*[OMIM107741]) $\epsilon 4$ are at high risk for cognitive decline and Alzheimer disease.^{1–3} However, the risk associated with *APOE* $\epsilon 4$ varies with other factors. The $\epsilon 4$ allele is more common among black than white individuals,^{4,5} and evidence^{6–12} suggests that, although the $\epsilon 4$ allele is a cognitive risk factor in both races,^{7,8} its effects are weaker in black persons.^{11,12} The cognitive impact of the $\epsilon 4$ allele also appears to be weaker in advanced older age^{6,13,14}; the $\epsilon 4$ allele is associated with a risk for cognitive decline and dementia among young-old individuals, but this association is no longer present among the oldest-old individuals, such as those 90 years or older studied by Corrada et al.¹⁴ A proportion of *APOE* $\epsilon 4$ carriers survives to 90 years or older still free of dementia,¹⁴ therefore appearing to be resilient to the deleterious effects of the allele. What factors might promote cognitive resilience among *APOE* $\epsilon 4$ carriers?

Previous work suggests that certain factors, such as higher educational levels, help to protect older adults with the neuropathologic features of Alzheimer disease from exhibiting cognitive decline.¹⁵ Such findings have been interpreted as supporting “cognitive reserve” theory, which posits that individuals with higher levels of reserve are better able to withstand aging and neuropathologic changes without showing cognitive decline.¹⁶ A similar

phenomenon may hold in the context of *APOE* $\epsilon 4$; modifiable factors may promote cognitive resilience among *APOE* $\epsilon 4$ carriers despite their high genetic risk. Identifying such factors could inform interventions for preventing or slowing cognitive decline among these high-risk individuals.

Using *APOE* $\epsilon 4$ as an indicator of high risk, we sought to identify factors that promote cognitive resilience in black and white carriers of the $\epsilon 4$ allele. We aimed to examine whether protective factors are different in black and white individuals because racial differences in the frequency and impact of *APOE* $\epsilon 4$ suggest racial differences may exist in what contributes to cognitive resilience to the $\epsilon 4$ allele. Among a comprehensive set of potential predictors, we specifically aimed to identify the factors most strongly predictive of cognitive resilience in black and white carriers of the $\epsilon 4$ allele to determine which factors may be most important to target in interventions for individuals at high genetic risk.

Methods

Population

This study was approved by the institutional review boards at the University of Pittsburgh, Pittsburgh, Pennsylvania; the University of Tennessee, Memphis; and the University of California, San Francisco. All participants gave written informed consent.

Participants were from the Health, Aging, and Body Composition (Health ABC) Study, a prospective cohort study of adults aged 69–80 years at baseline. Health ABC Study participants were recruited from a random sample of white older adults and every black older adult who were Medicare eligible, community dwelling, and living in Pittsburgh or Memphis. Three thousand seventy-five individuals were enrolled. The baseline (year 1) study visits occurred from May 1997 to June 1998. Individuals were required to be well functioning at baseline (no difficulty with activities of daily living, including the ability to walk 0.4 km and to climb 10 stairs without resting) to be included. Additional details about the study participants are included in prior Health ABC Study reports.^{17–19}

Of the 3075 Health ABC Study participants, 2487 individuals (992 black and 1495 white) were free of prevalent cognitive impairment (defined as a baseline Modified Mini-Mental State Examination [3MS] score more than 1.5 SDs below the mean compared with peers of the same race) and underwent repeated cognitive testing (2 or more 3MS assessments) over 11 years (through 2008). Of these, 2349 individuals (924 black and 1425 white) underwent *APOE* genotype testing from standard single-nucleotide polymorphism analyses, with 670 (28.5%) being *APOE* $\epsilon 4$ carriers (329 black carriers [35.6%] and 341 white carriers [23.9%]). These 670 *APOE* $\epsilon 4$ carriers (ie, those possessing 1 $\epsilon 4$ allele) served as our primary analytic cohort.

Measures

Cognition and Cognitive Resilience—Cognitive functioning was assessed at years 1, 3, 5, 8, 10, and 11 with the 3MS.²⁰ With scores ranging from 0 to 100, the 3MS assesses orientation, attention, memory, construction, basic language, verbal fluency, and

conceptualization and is more sensitive than the traditional Mini-Mental State Examination.²¹

As depicted in Figure 1, we used data from the entire Health ABC Study cohort to classify *APOE* $\epsilon 4$ carriers as cognitively resilient vs nonresilient. We created our definition to investigate the following question: How do some $\epsilon 4$ carriers maintain cognitive health to the extent that their cognitive trajectories resemble those of the most cognitively healthy *APOE* $\epsilon 4$ noncarriers? First, we considered cognitive trajectory data from the entire Health ABC Study cohort to contextualize normative cognitive change for all participants during the follow-up period. Among the 2487 Health ABC Study participants without baseline cognitive impairment and with repeated 3MS testing, we constructed linear mixed-effects regression models to characterize individuals' longitudinal cognitive trajectory using all their 3MS scores (baseline through the last score) stratified by race and adjusted for age group (69–72, 73–76, and 77–80 years) and sex. This analysis calculated each individual's 3MS slope deviation from that of their demographically similar peers. Next, we compared the individual cognitive trajectories of the *APOE* $\epsilon 4$ carriers with those from the entire Health ABC Study cohort to define resilience. We classified *APOE* $\epsilon 4$ carriers as *resilient* if their cognitive trajectory fell within the highest tertile compared with demographically similar individuals in the entire cohort (ie, best retained cognition) and as *nonresilient* if their cognitive trajectory fell within the lowest 2 tertiles (ie, greatest decline in cognition). We reasoned that comparing *APOE* $\epsilon 4$ carriers with the entire cohort would yield a more representative classification of resilience than would basing our definition on the *APOE* $\epsilon 4$ carriers alone. We made this classification conservatively based on the highest tertile because no clinical cutoff has been established to define cognitive resilience. For descriptive purposes, eTable 1 in the Supplement lists 3MS change values that correspond to the top tertile cut point defining resilience for each demographic group.

Demographic Characteristics, Literacy, and Financial Status—Participants' age, race, sex, and educational level (less than high school and high school graduate and/or some college vs college graduate) were collected at baseline. Participants were classified as having a higher financial status at baseline if they endorsed 2 or more of the following: the amount of money they have meets their needs very well; they have money left over at the end of the month; or they own their apartment or house. Literacy was assessed shortly after baseline with the Rapid Estimate of Adult Literacy in Medicine, a word-reading test that yields reading grade-level equivalents.²²

Comorbidities and Health Factors—Self-report, medications, physician diagnoses, laboratory values, and clinical measurements were used to characterize baseline comorbidities, including hypertension, diabetes mellitus, history of stroke, and history of myocardial infarction. Individuals with a body mass index greater than 30 (calculated as the baseline weight in kilograms divided by height in meters squared) were considered obese. High cholesterol levels were defined as total cholesterol levels of at least 240 mg/dL (to convert to millimoles per liter, multiply by 0.0259). Individuals whose C-reactive protein and interleukin 6 values were greater than the median were classified as having high levels of inflammation.²³ Participants completed the Center for Epidemiologic Studies–Depression

Scale²⁴; scores of at least 16 were considered to indicate depression. Participants self-reported the typical number of hours they slept per night (coded as 6, 7, and 8 hours).

Lifestyle and Psychosocial Factors—At baseline, participants reported their marital status, whether they lived alone, and whether they visited friends or family regularly (defined as at least twice per week). They answered yes/no questions²⁵ assessing whether they had experienced major negative life events during the past year (ie, whether a close friend or family member had a serious accident or illness; whether a spouse or partner died; whether a child, grandchild, close friend, or relative died; whether a pet died; whether a relationship with a family member or close friend changed for the worse; whether the participant or a family member was assaulted or robbed; or whether a close friend or family member was arrested or had trouble with the law). Participants were coded as endorsing no negative life events vs any. Participants reported whether they were working or volunteering and how many hours per week they spend reading (classified as low, moderate, and avid reading based on tertiles). Participants self-reported physical activity; total weekly energy expenditure was calculated as kilocalories per kilogram per week and was used to classify participants as having low, moderate, or high energy expenditure based on tertiles. Participants reported their current alcohol use and smoking status.

Statistical Analysis

As shown in eTable 2 in the Supplement, the 2 racial groups differed by many characteristics, providing further justification for racial stratification of the following analyses. To examine predictors of cognitive resilience among *APOE* ε4 carriers, we first evaluated bivariate associations between participant characteristics and resilience using χ^2 tests separately by race. Next, among all our potential predictors, we investigated which factors were most strongly predictive of resilience in a multivariable fashion using random forest analyses among race strata. Random forest analysis²⁶ is a nonparametric approach capable of handling a large number of potential predictor variables. Random forest analysis uses a series of classification or regression trees to evaluate multiple potential predictors within the same analysis and to rank variables according to their importance in predicting the outcome. A set of classification trees are created, each based on a random sample of participants, and a random sample of potential predictor variables are evaluated a teach split in the tree. Results are combined across trees to produce a rank order list of important predictor variables, and aggregating tree results in this manner yields more robust findings than those produced by a single tree.²⁶ We conducted random forest analyses in the R environment²⁷ using the “party” package,^{28–30} which applies a conditional measure of variable importance to handle correlated predictor variables.²⁶ Our forest consisted of 5000 trees, and at each potential split we evaluated a random sample of 10 predictors. Variables were ranked by an importance score, reflecting the relative strength of each variable in predicting the outcome. We followed the criteria recommended by Strobl et al²⁶ for considering a variable to be an important predictor. As a complementary multivariable analysis, we constructed logistic regression models that included all variables considered to be important predictors in the random forest results. This analysis elucidates the effects of each of these predictors by quantifying the independent effect of each predictor on cognitive resilience.

Results

Verification of *APOE* $\epsilon 4$ Status as a Risk Factor in Both Races

Before conducting our primary analyses, we verified whether *APOE* $\epsilon 4$ status was a risk factor among both races in the Health ABC Study cohort by examining the effect of the $\epsilon 4$ allele on cognitive trajectory separately by race using linear mixed models. As anticipated, *APOE* $\epsilon 4$ carriers had worse cognitive change among black ($\beta = -0.21$; $P < .001$) and white ($\beta = -0.33$; $P < .001$) groups; these associations remained ($P < .001$ for both) after adjustment for all our examined variables.

Associations Between Participant Characteristics and Cognitive Resilience in *APOE* $\epsilon 4$ Carriers

Among white *APOE* $\epsilon 4$ carriers, the following characteristics were associated with being cognitively resilient in bivariate analyses (Table 1): older age, a higher educational level, a higher literacy level, the absence of diabetes mellitus, the absence of obesity, having no negative life events in the past year, and more time spent reading ($P < .05$ for all). The multivariable random forest analysis for white *APOE* $\epsilon 4$ carriers showed very strong model classification performance (C statistic, 0.86), and the strongest predictors of resilience in rank order were (1) no negative life events, (2) higher literacy levels, (3) older age, (4) higher educational level, and (5) more time spent reading (Figure 2).

Among black *APOE* $\epsilon 4$ carriers, female sex, higher educational level, higher literacy level, fewer hours of sleep per night, regularly visiting friends or family, and working or volunteering were associated with being cognitively resilient in bivariate analyses ($P < .05$ for all; Table 2). The random forest analysis for black *APOE* $\epsilon 4$ carriers showed very strong model classification performance (C statistic, 0.83), and the strongest predictors of resilience in rank order were (1) higher literacy levels, (2) higher educational level, (3) female sex, and (4) absence of diabetes mellitus (Figure 2).

The independent effects of these variables on resilience in both races are presented in Table 3 and are based on a multivariable logistic regression model including the most important predictors identified in the random forest analyses. In sensitivity analyses, we repeated the random forest analyses excluding *APOE* $\epsilon 4$ homozygous carriers in our cohort (19 white and 29 black participants), and results were similar to those of our primary analyses.

Discussion

We identified a number of factors predictive of cognitive resilience among *APOE* $\epsilon 4$ carriers. The factors most strongly predictive of resilience among white *APOE* $\epsilon 4$ carriers included no recent negative life events, higher literacy levels, older age, higher educational level, and more time spent reading (in relative order of importance). Among black *APOE* $\epsilon 4$ carriers, the factors most strongly predictive of resilience included higher literacy level, higher educational level, female sex, and the absence of diabetes mellitus (in relative order of importance). These findings raise the possibility that interventions targeting the modifiable factors among these predictors could help promote cognitive resilience in *APOE* $\epsilon 4$ carriers.

By investigating cognitive resilience in black and white *APOE* $\epsilon 4$ carriers, we found similarities and differences between racial groups for the factors that best protect individuals against the deleterious effects of the $\epsilon 4$ allele. Among both races, factors thought to be markers of cognitive reserve¹⁶ stood out as strong predictors of resilience, including higher literacy and educational levels in both racial groups and greater cognitive activity (time spent reading) among white carriers. These findings provide further evidence of the beneficial role of cognitive reserve in aging, specifically that greater reserve is protective even among individuals at high genetic risk for decline.³¹

The pattern of predictors between racial groups diverged for other factors. Among white *APOE* $\epsilon 4$ carriers, we found an absence of negative life events to be the strongest predictor of resilience, but this relationship was not apparent among black carriers. These findings mirror those of a recent study³² that identified stress as a cognitive risk factor among white, but not black, older adults regardless of *APOE* $\epsilon 4$ status. Stress in aging can have negative effects on memory and the structure of the hippocampus,³³ but mechanisms driving potential racial differences in the influence of stress on cognitive aging remain unclear. Future research might explore whether the following differ by race: (1) types of stressors experienced in aging, (2) older adults' coping styles, and (3) the neurobiological effects of stress on the aging brain.

Another area where patterns appeared to differ by race was the relative strength of the influence of cardiovascular factors. Among black *APOE* $\epsilon 4$ carriers, the absence of diabetes mellitus was among the strongest predictors of resilience, whereas the association between cardiovascular factors and resilience was less clear in white *APOE* $\epsilon 4$ carriers (although the absence of diabetes mellitus and obesity was associated with resilience in bivariate analyses for white carriers, no cardiovascular health factors were identified as strong predictors in our multivariable analysis). Overall, results suggest possible complex racial differences in what promotes resilience among *APOE* $\epsilon 4$ carriers. Although our study suggests that the relative importance of factors in promoting resilience varies by race, the mechanisms behind racial differences remain unclear and should be explored in future research. Racial differences in participant characteristics may in turn influence racial differences in which factors contribute to cognitive resilience.

A few factors associated with cognitive resilience were counterintuitive. We found that older age was predictive of resilience in white *APOE* $\epsilon 4$ carriers, a pattern consistent with previous findings that the cognitive impact of the $\epsilon 4$ allele lessens once individuals reach advanced age.^{6,14} In contrast to evidence of the $\epsilon 4$ allele being a stronger risk factor for Alzheimer disease in women compared with men,³⁴ we found that black female *APOE* $\epsilon 4$ carriers were more likely to be resilient than their male counterparts, a discrepancy that may be influenced by race effects. Among black carriers, we found a bivariate association between sleep and resilience, suggesting that shorter sleep duration was protective. Although the direction of this relationship is surprising, other studies have been mixed in identifying long and short sleep durations as cognitive risk factors.^{35,36} However, given that an association between sleep duration and resilience did not hold up in our multivariable analyses, the observed bivariate association may have been driven by other factors.

Similar to previous studies of predictors of cognitive outcome in *APOE* $\epsilon 4$ carriers,^{37,38} we found that multiple domains influence the cognitive trajectory of *APOE* $\epsilon 4$ carriers, including demographics, cognitive reserve, and other psychosocial and health factors. Limitations of prior studies include a lack of investigation of the potential for racial differences in what predicts cognitive outcome in *APOE* $\epsilon 4$ carriers or examination of a limited number of potential predictors. The strengths of our study include our ability to explore a comprehensive set of factors in a well-characterized prospective cohort of black and white older adults. Another strength is our application of a novel multivariable analysis to reveal the factors most strongly predictive of resilience and thus those most important to target in interventions. We were also able to use the entire Health ABC Study cohort to contextualize normative cognitive change across 11 years and use this context as a reference in defining cognitive resilience among *APOE* $\epsilon 4$ carriers. A main limitation of our study is that some of our predictors were based on self-report; thus, future studies would benefit from the use of objective measures of sleep and physical activity, for example. In addition, our study does not capture *APOE* $\epsilon 4$ carriers whose cognitive decline may have begun before 69 years of age (before our baseline); thus, we do not know how a survival effect may have influenced our findings.

Conclusions

A number of factors appear to help minimize the deleterious effect of the $\epsilon 4$ allele on cognition in aging, although *APOE* $\epsilon 4$ carriers are a high-risk group. Future directions include investigating interventions geared toward promoting cognitive resilience in *APOE* $\epsilon 4$ carriers by targeting the modifiable factors we found to be predictors of resilience. Enhancing cognitive reserve appears to be an important intervention target in black and white *APOE* $\epsilon 4$ carriers. Our study provides preliminary evidence that other top intervention targets may vary by racial group. For example, although an intervention designed for white *APOE* $\epsilon 4$ carriers may benefit from a greater focus on stress reduction or stress management, an intervention designed for black *APOE* $\epsilon 4$ carriers may benefit from a greater focus on cardiovascular health (eg, management of diabetes mellitus). Our results also suggest that interventions designed to target more than 1 domain concurrently, such as those addressing cognitive reserve and psychosocial or health factors within the same program, could have greater cognitive benefit.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Role of the Funder/Sponsor: The NIA was involved in the design and conduct of the study; data collection and management; and the review and approval of the manuscript.

Group Information

Principle investigators for the ABC Health Study included Tamara B. Harris, MD, National Institute on Aging (lead investigator); Melissa E. Garcia, MPH, National Institute on Aging; Anne B. Newman, MD, MPH, University of Pittsburgh, Pittsburgh, Pennsylvania; Suzanne Satterfield, MD, DrPH, University of Tennessee, Memphis; Steven R. Cummings, MD, University of California, San Francisco; and Michael C. Nevitt, PhD, University of California, San Francisco. Health ABC Study coordinators were Diane Ives, MPH, University of Pittsburgh, and Jan Elam, BS, University of Tennessee, Memphis. Health ABC project director was Susan M. Rubin, MPH, University of California, San Francisco.

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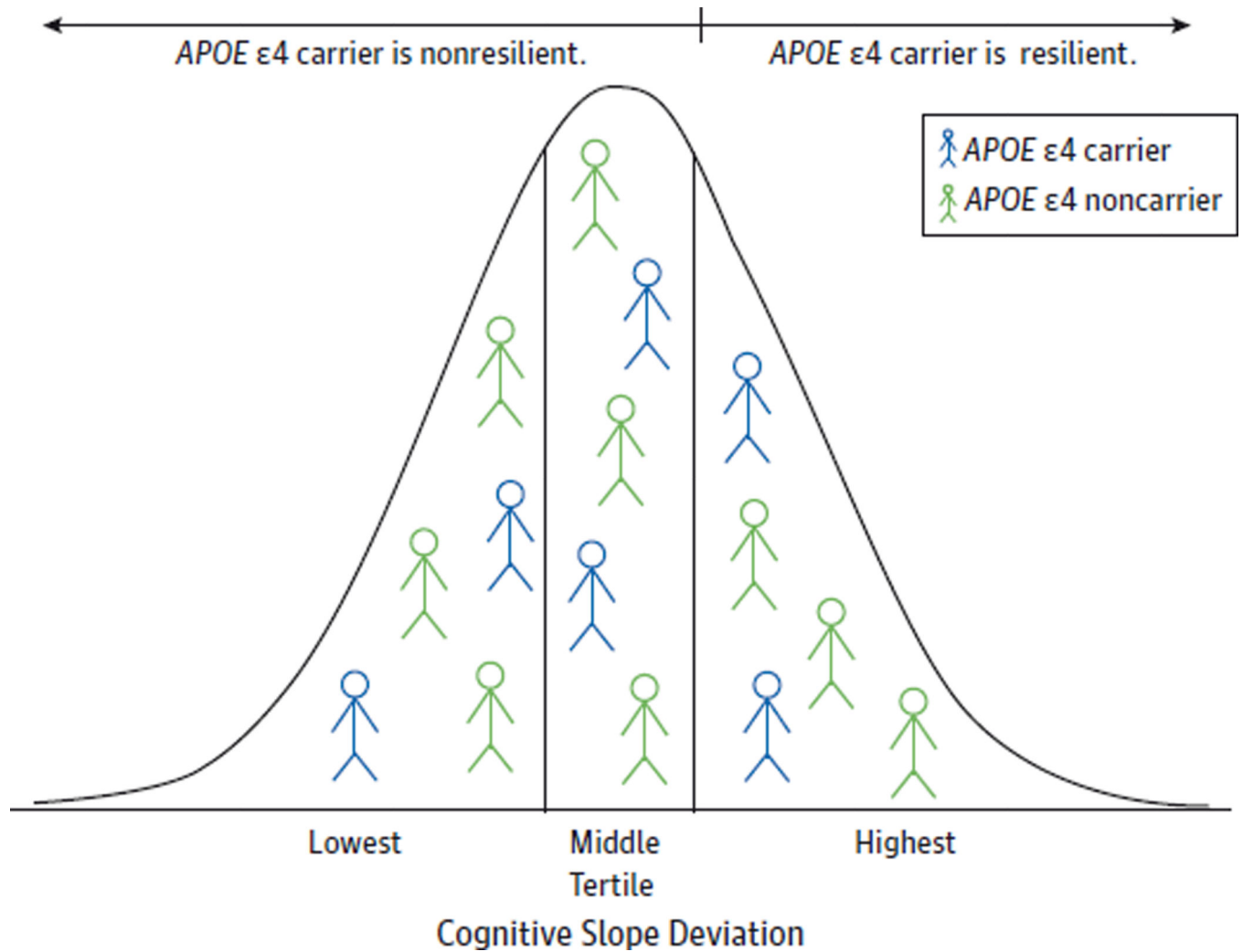


Figure 1.

Defining Cognitive Resilience for Apolipoprotein E ($APOE$) $\epsilon 4$ Carriers

Graphic representation of how $APOE$ $\epsilon 4$ carriers ($n = 670$) were classified as cognitively resilient vs nonresilient by comparing the cognitive trajectories of the carriers with those of demographically similar individuals (curve) in the entire Health, Aging, and Body Composition (Health ABC) Study cohort ($n = 2487$). The numbers of person-figures do not correspond directly to any real numbers.

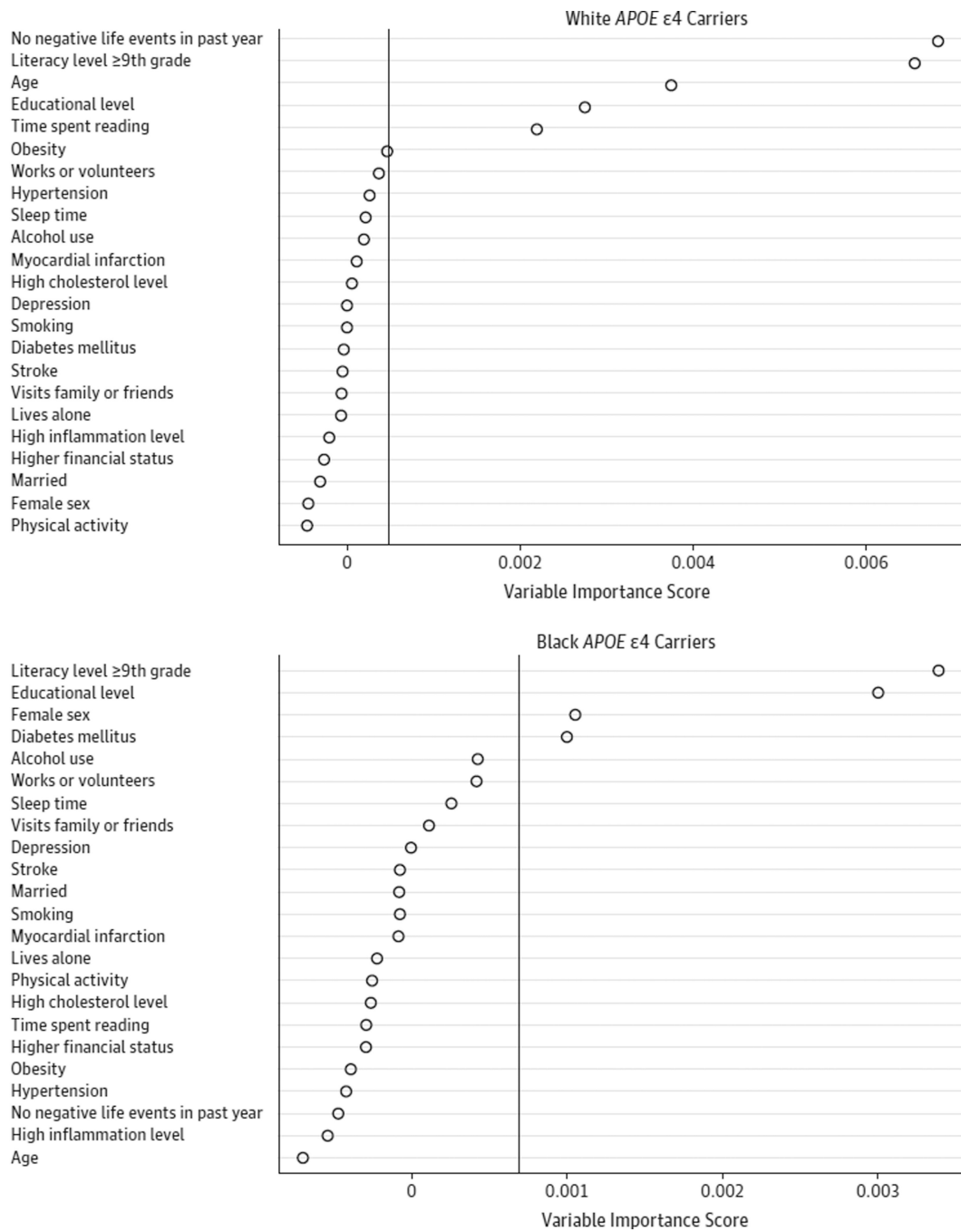


Figure 2. Random Forest Analyses to Identify the Strongest Predictors of Cognitive Resilience
 Random forest results identify the strongest predictors of cognitive resilience among 272 white and 258 black carriers of apolipoprotein E (*APOE*) ε4 who had complete data for all examined variables. Variables are ranked by their relative importance in predicting resilience using a variable importance score.²⁶ Variables to the right of the vertical line are considered important predictors.

Table 1

Bivariate Associations: Potential Predictors of Cognitive Resilience Among White *APOE* ϵ 4 Carriers

Characteristic	Study Participants, % ^a			P Value
	All (N = 341)	Resilient (n = 89)	Nonresilient (n = 252)	
Age, y				
69–72	40.8	29.2	44.8	
73–76	44.0	55.1	40.1	.03 ^b
77–80	15.2	15.7	15.1	
Female sex	47.5	52.8	45.6	.24
Educational level				
Did not graduate high school	11.1	3.4	13.9	
High school graduate and/or some college	58.4	47.2	62.3	<.001 ^b
College graduate	30.5	49.4	23.8	
Literacy level 9th grade	84.2	97.8	79.4	<.001 ^b
Higher financial status	75.9	82.6	73.6	.09
Hypertension	49.0	44.9	50.4	.38
Diabetes mellitus	12.9	5.6	15.5	.02 ^b
Stroke	8.0	7.9	8.0	.96
Myocardial infarction	12.2	15.9	10.9	.22
Obesity	15.8	7.9	18.7	.02 ^a
High cholesterol level ^c	19.5	21.4	18.8	.60
High inflammation level	20.8	18.0	21.8	.44
Depression ^d	4.7	4.6	4.8	.93
Sleep time, h/night				
6	33.7	28.4	35.6	
7	29.9	33.0	28.7	.46
8	36.4	38.6	35.6	
Married	66.1	67.1	65.8	.84
Living with someone	75.9	79.6	74.6	.35
Regularly visits family or friends ^e	83.2	84.3	82.9	.76
Lack of negative life events in past year	32.8	42.7	29.4	.02 ^b
Works or volunteers	60.4	68.5	57.5	.07
Time spent reading, h/wk				
<7 (Low)	26.9	15.7	31.0	
7–14 (Moderate)	49.2	56.2	46.7	.02 ^a
>14 (Avid)	23.9	28.1	22.3	
Physical activity, kcal/kg/wk				
<45.7 (Low)	24.9	21.4	26.2	.32

Characteristic	Study Participants, % ^a			P Value
	All (N = 341)	Resilient (n = 89)	Nonresilient (n = 252)	
45.7–88.9 (Moderate)	39.9	37.1	40.9	
>88.9 (High)	35.2	41.6	32.9	
Current alcohol use ^f	61.1	67.1	59.0	.18
Current nonsmoker	94.7	97.8	93.7	.14

Abbreviation: *APOE*, apolipoprotein E.

^a Percentages have been rounded and may not total 100.

^b Indicates significance at $P < .05$.

^c Indicates total cholesterol level of 240 mg/dL or greater (to convert to millimoles per liter, multiply by 0.0259).

^d Indicates Center for Epidemiologic Studies–Depression Scale score of 16 or greater.

^e Indicates at least twice per week.

^f Indicates at least 1 drink per week.

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Table 2Bivariate Associations: Potential Predictors of Cognitive Resilience Among Black *APOE* ϵ 4 Carriers

Characteristics	Study Participants, % ^a			P Value
	All (N = 329)	Resilient (n = 98)	Nonresilient (n = 231)	
Age, y				
69–72	45.9	40.8	48.1	
73–76	38.9	38.8	39.0	.19
77–80	15.2	20.4	13.0	
Female sex	62.9	71.4	59.3	.04 ^b
Educational level				
Did not graduate high school	37.8	18.4	46.1	
High school graduate and/or some college	46.0	61.2	39.6	<.001 ^b
College graduate	16.2	20.4	14.4	
Literacy level 9th grade	54.1	74.5	45.5	<.001 ^b
Higher financial status	45.1	52.6	41.9	.08
Hypertension	66.3	64.3	67.1	.62
Diabetes mellitus	24.3	18.4	26.8	.10
Stroke	8.3	9.4	7.9	.65
Myocardial infarction	10.7	12.2	10.0	.55
Obesity	37.7	35.7	38.5	.63
High cholesterol level ^c	20.1	23.7	18.6	.29
High inflammation level	33.1	28.6	35.1	.25
Depression ^d	3.4	2.0	4.0	.38
Sleep time, h/night				
6	50.0	59.4	46.0	
7	20.4	21.9	19.8	.02 ^b
8	29.6	18.8	34.2	
Married	38.7	42.6	37.1	.36
Living with someone	64.9	68.4	63.4	.39
Regularly visits family or friends ^e	84.8	91.8	81.8	.02 ^b
No negative life events in past year	31.0	28.6	32.0	.53
Works or volunteers	53.2	63.9	48.7	.01 ^b
Time spent reading, h/wk				
<7 (Low)	42.5	36.6	45.1	
7–14 (Moderate)	42.8	43.0	42.7	.13
>14 (Avid)	14.7	20.4	12.2	
Physical activity, kcal/kg/wk				
<45.7 (Low)	35.0	28.6	37.7	.29

Characteristics	Study Participants, % ^a			P Value
	All (N = 329)	Resilient (n = 98)	Nonresilient (n = 231)	
45.7–88.9 (Moderate)	32.8	35.7	31.6	
>88.9 (High)	32.2	35.7	30.7	
Current alcohol use ^f	36.8	36.7	36.8	.99
Current nonsmoker	84.5	89.8	82.3	.08

Abbreviation: *APOE*, apolipoprotein E.

^a Percentages have been rounded and may not total 100.

^b Indicates significance at $P < .05$.

^c Indicates total cholesterol level of 240 mg/dL or greater (to convert to millimoles per liter, multiply by 0.0259).

^d Indicates Center for Epidemiologic Studies–Depression Scale score of 16 or greater.

^e Indicates at least twice per week.

^f Indicates at least 1 drink per week.

Table 3

Results of Multivariable Logistic Regression Models Examining Most Important Predictors of Cognitive Resilience^a

Predictor	Resilience, OR (95% CI)
Model 1: white <i>APOE</i> ε4 carriers (n = 331)	
No negative life events in past year	1.75 (1.00–3.03)
Literacy level 9th grade	9.50 (2.67–60.89)
Age group compared with 69–72 y	
73–76 y	2.01 (1.13–3.63)
77–80 y	1.87 (0.82–4.18)
Educational level compared with did not graduate high school	
High school graduate and/or some college	1.77 (0.55–7.99)
College graduate	3.81 (1.13–17.56)
Time spent reading compared with low reading level ^b	
Moderate	1.91 (0.96–4.00)
Avid	1.36 (0.62–3.07)
Model 2: black <i>APOE</i> ε4 carriers (n = 328)	
Literacy level 9th grade	2.27 (1.29–4.06)
Educational level compared with did not graduate high school	
High school graduate and/or some college	2.86 (1.54–5.49)
College graduate	2.52 (1.14–5.62)
Diabetes mellitus	0.69 (0.36–1.26)
Female sex	1.42 (0.83–2.47)

Abbreviations: *APOE*, apolipoprotein E; OR, odds ratio.

^a Models included all variables that were identified in the random forest analyses as being important predictors of cognitive resilience. To be included in these analyses, participants were required to have complete data for all variables included in the model.

^b Levels of reading were defined as low (<7 h/wk), moderate (7–14 h/wk), and avid (≥14 h/wk).