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Apolipoprotein E Genotype and Memory in the Sixth Decade of Life

Mark R. Schultz, M.A.[1], **Michael J. Lyons, Ph.D.**[1], **Carol E. Franz, Ph.D.**[2], **Michael D. Grant, Ph.D.**[1], **Corwin Boake, Ph.D.**[3], **Kristen C. Jacobson, Ph.D.**[4], **Hong Xian, Ph.D.**[5,6], **Gerard D. Schellenberg, Ph.D.**[7,8,9], **Seth A. Eisen, M.D., M.Sc.**[5,6,10,11], and **William S. Kremen, Ph.D.**[2,12]

[1] Department of Psychology, Boston University

[2] Department of Psychiatry, University of California, San Diego

[3] The Institute for Rehabilitation and Research, Houston, TX

[4] Department of Psychiatry, University of Chicago

[5] Research Service, St. Louis VA Medical Center

[6] Department of Internal Medicine, Washington University School of Medicine

[7] VA Puget Sound Healthcare System

[8] Division of Gerontology and Geriatric Medicine, Department of Medicine, University of Washington

[9] Departments of Neurology and Pharmacology, University of Washington

[10] Medical Service, St. Louis VA Medical Center

[11] Department of Psychiatry, Washington University School of Medicine

[12] Center for Behavioral Genomics, University of California, San Diego

Abstract

Background—Virtually all adult studies of *APOE* genotypes and cognition have included individuals over 60. In older adults, ε4 carriers may manifest greater cognitive asymmetries than non-ε4 carriers even in the absence of overall mean differences. General cognitive ability may also be affected by aging and APOE genotype, but most studies have inadequately addressed this potential confound. The goals of this study were to examine, in middle age, the relationship of *APOE* genotype with episodic memory and verbal-visuospatial episodic memory asymmetries, after accounting for prior general cognitive ability.

Method—We compared ε4+ and ε4- individuals in 626 male twins in their 50s. We examined verbal and visuospatial episodic memory and verbal-visual asymmetry scores after adjusting for cognitive ability at age 20. Analyses corrected for correlations between twin pair members.

Results—Compared with ε4- individuals, ε4 carriers performed significantly more poorly on verbal, but not visuospatial memory, manifested significantly greater cognitive asymmetry, and also had significantly more concerns about memory. At age 20, ε4 carriers had higher general

Correspondence: Dr. William S. Kremen, Department of Psychiatry, Center for Behavioral Genomics, University of California, San Diego, 9500 Gilman Drive (MC 0738), La Jolla, CA 92093-0738, Tel: 858-822-2393, Fax: 858-822-5856, wkremen@ucsd.edu.

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cognitive ability than ε4- individuals, and current memory differences were enhanced after adjusting for age 20 cognitive ability.

Conclusions—Small, but significant, *APOE*-ε4-related memory deficits do appear in the sixth decade of life in individuals who show no signs of preclinical dementia. The results partially support studies of older adults that suggest that increased cognitive asymmetries reflect risk for dementia and are associated with the *APOE*-ε4 genotype. The results also highlight the potential problems of not having accurate data on prior cognitive ability.

Episodic memory is the most prominent cognitive deficit in Alzheimer's disease (AD). Despite widespread agreement that the Apolipoprotein (*APOE*)-ε4 allele contributes to risk for AD (1), the question of whether the presence of an ε4 allele influences episodic memory directly or influences neurodegenerative processes that lead to memory deficits associated with AD remains unresolved. Several factors may contribute to inconsistencies regarding the association of ε4+ status with cognitive deficits in individuals without dementia, or its impact at different ages. Inclusion of preclinical or prodromal AD cases in ε4+ groups may make it difficult to determine whether there are direct effects of ε4 on cognition (2, 3); this issue may be of particular concern in clinic samples. Several studies with a relatively low mean age still often had an age range that included older adults (4, 5), thus making it difficult to know the extent to which *APOE* genotype differences were present in the younger participants. In a meta-analysis of the cognitive effects of *APOE* genotype, only 14% of studies examining general cognitive ability and 21% of studies examining episodic memory had mean ages that were below 60 (1). The meta-analytic results did indicate that the correlation between effect size and the average age in each study was .20 for general cognitive ability and .18 for episodic memory, but there were not enough studies for those effects to reach statistical significance (1). In old-old adults, this pattern of ε4 differences may even be reversed, with ε4- individuals performing more poorly than ε4+ individuals (6). The relative under-representation of middle-aged participants in studies and the possibility that the effect of *APOE* genotype on cognition may have a nonlinear relationship with age suggest that simply using age as a covariate may be insufficient. It would, thus, be advantageous to directly study a large sample of adults under 60. We are aware of only one such study, and they did find significant episodic memory deficits in ε4 carriers (7).

Despite the lack of studies of solely middle-aged adults, there have been two studies of children. In one, there was no difference in *APOE* genotype frequencies among high and average IQ children (8). In the other, effect sizes for general cognitive ability differences between ε4+ and ε4- participants at age 11 were .20, although these differences did not reach statistical significance (9). Thus, there is still a need to explore the question of how early the cognitive effects of the ε4 allele are manifested.

Other issues that are relevant for APOE studies include matching for overall cognitive ability, the meaning of cognitive asymmetries, and the presence of subjective concerns about memory. Meta-analytic results indicate that reduced general cognitive ability in adults tends to be associated with the ε4 allele (1), but this pattern may also be a potential methodological problem. These findings raise questions about the validity of equating ε4+ and ε4- groups on general cognitive ability in older samples, and they suggest that—when possible—researchers should take into account differences that may have been present earlier in life.

Some studies of non-demented older adults have focused on cognitive asymmetries as a predictor of AD. Cognitive asymmetries are essentially neuropsychological probes of asymmetries between left and right cerebral hemisphere function. Greater asymmetries based on absolute differences between tests that tap primarily left versus right hemisphere function have been observed in ε4+ compared with ε4- groups (10, 11). Significantly greater

than normal asymmetries are thought to reflect abnormalities in brain function, as suggested by the consistency of these comparisons of ε4+ and ε4- groups with the lateralized cognitive deficits and structural brain asymmetries that are frequently observed in early AD (12).

Some evidence has also suggested that memory complaints in cognitively intact older adults were associated with a greater rate of cognitive decline in three-to-six-year follow-ups (13). Being positive for both memory complaints and the *APOE*-ε4 genotype was associated with twice the cognitive decline of those who had neither.

Given these considerations, we were interested in comparing episodic memory performance in ε4+ and ε4- middle-aged men who were in their 50s, taking into account their prior general cognitive ability at—on average—age 20. We also tested whether the ε4 allele was associated with greater cognitive asymmetries for verbal and visuospatial memory, and greater subjective memory concerns in these non-demented individuals under the age of 60.

Methods

Participants

The study sample consisted of participants in wave 1 of the Vietnam Era Twin Study of Aging (VETSA), a longitudinal behavior genetic study of aging (14). Participants were male twins who were randomly drawn from the Vietnam Era Twin (VET) Registry; VET Registry twins were born between 1939 and 1957 and had both served in the United States military during the Vietnam era (1965–1975) (15, 16). Zygosity was determined by a combination of questionnaire and blood group methods, an approach that has been demonstrated to be 95% accurate as measured against DNA analysis (17). VETSA participants were randomly selected from 3,322 VET Registry twin pairs who participated in a telephone survey in 1992 (18). Participants in the 1992 study were not selected on the basis of any demographic or diagnostic characteristics. They currently live throughout the U.S., making this a national sample. Both the larger sample and the VETSA sample are representative of American men in this age range based on U.S. census data (14).

The present analyses are based on 626 VETSA participants with *APOE* genotype data. VETSA data collection and genotyping is still ongoing. Participants' mean age was 55.3 ± 2.3 years; all participants were in their 50s at the time of recruitment, but five individuals turned 60 by the time of testing. Mean education was 13.9 ± 2.1 (range 4 – 20) years, with 98.2% (n=616) having earned at least a high school degree. In terms of ethnicity, 95.5% were white, non-Hispanic, 3.8% were African-American, 0.3% were Hispanic, and 0.3% were "other." A total of 76.4% (n=478) were employed full-time and 8.1% (n=52) were retired. There were 500 (79.9%) individuals who were married at the time of assessment, 61 (9.7%) who were divorced, and 46 who were single. Total combined family income averaged between $50,000 and $60,000.

Measures

Episodic memory—Verbal episodic memory was assessed with the Wechsler Memory Scale (WMS-III) Logical Memory subtest, which consists of two stories read to participants for immediate and delayed free recall (19). In the standard administration, the second story is presented twice prior to the delayed recall, but it was presented only once prior to the delay condition in our administration. Visuospatial episodic memory was assessed with the WMS-III Visual Reproductions subtest, which consists of five designs that are presented for 10 seconds each and then drawn from memory. This immediate condition is followed by a delayed recall conditions. Logical memory and visual reproductions are both sensitive to cognitive deterioration associated with dementia (20). Composite verbal and visuospatial

memory scores were created by taking the mean of the immediate and delayed recall conditions. Cognitive asymmetry scores were computed by converting logical memory and visual reproductions scores into *z*-scores, and calculating the logical memory minus visual reproductions *z*-score difference.

General cognitive ability—Because general cognitive ability is associated with memory and other cognitive abilities (21, 22), logical memory and visual reproduction scores were adjusted for prior general cognitive ability. Our index of general cognitive ability was the Armed Forces Qualification Test (AFQT), which was administered as a screening instrument just prior to military induction when the average age of participants in the present analyses was 19.9 (± 1.37) and again during the VETSA at average age 55.1. The AFQT is a 50-minute paper-and-pencil test consisting of 100 multiple-choice items with equal numbers of items assessing the domains of vocabulary, arithmetic, spatial processing (matching folded or unfolded box patterns), and matching/reasoning about tools and equipment (23). It is highly correlated with other measures of general cognitive ability (24); after correcting for restriction of range, the AFQT was correlated .84 with the Wechsler Adult Intelligence Scale and .85 with the Multidimensional Assessment Battery (25, 26). Total AFQT scores from the time of induction into the military were available from military records. AFQT scores are reported as percentiles; they can range from 10 to 99 because individuals scoring below the 10^{th} percentile were statutorily excluded from the military.

Subjective memory concerns—Participants were asked to rate an item about memory concerns ("I worry about my memory") on a five-point scale (1=Definitely True, 2=Mostly True, 3=Mostly False, 4=Definitely False, 5=Don't Know). Those whose response was 5 were not included in the analysis with this variable.

Depressive symptoms—Memory concerns could reflect a depressive bias rather than an objective appraisal about memory difficulties. Therefore, we compared the ε4+ and ε4- on the Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D (27) is a widely used and well-validated, 20-item scale with questions about depressive mood and behavior during the past week. Scores on the CES-D were positively skewed. Consequently, we used a log transformation (log [CES-D score] + 1) and the analysis was performed on the transformed scores.

APOE Genotyping

APOE genotypes were determined using previously described polymerase chain reaction (PCR) conditions (28) and the HhaI restriction digest method (29) in the laboratory of Dr. Schellenberg at the Puget Sound VA Healthcare System. All genotypes were independently determined twice by laboratory personnel blind to the initial genotype and to the identity of the co-twin. Genotype information was available on 626 of the 746 VETSA participants (84%) at the time of this analysis. Among these 626 individuals, 189 (30.2%) possessed at least one ε4 allele and 437 (69.8%) did not. There were 13 pairs (2.1%) that were ε4 homozygous; .1% were ε2 homozygous and 49.3% were ε3 homozygous. Due to the low rate of ε4 homozygosity, we divided the sample into two groups: ε4+ (individual least one ε4 allele) and ε4- (no ε4 alleles). Participants were unaware of their APOE genotype.

Procedure

Participants traveled either to the University of California, San Diego or Boston University to participate in a full day of cognitive and biomedical assessments. Blood samples were obtained in the morning on the day of testing and were shipped to the Puget Sound VA laboratory. The neuropsychological tests were part of a larger assessment battery. The study was approved by the Institutional Review Boards of all of the participating institutions,

written informed consent was obtained from all participants, and all were paid for their participation in the study.

Statistical Analysis

The 626 individuals in the sample included 350 monozygotic and 276 dizygotic twins, some of whom were members of the same twin pair and some of whom were unpaired. The proportion of monozygotic and dizygotic twins was similar in the ε4+ (54%) and ε4- (60%) groups; however, the analyses performed for this study were not twin analyses. We utilized multilevel (mixed) linear modeling (SPSS version 11.5); this procedure allowed us to utilize all available data and statistically adjust for the expected non-independence of observations. The mixed model incorporates both fixed and random effects parameters (30, 31). The simplest model (one with no explanatory variables) is parameterized as follows: $Y_{ij} = \beta_0 + u_j + e_{ij,}$ where Y_{ij} is the outcome variable for individual i in twin pair j, β_0 is the intercept (a fixed effect), u_j is the twin pair-specific random effects representing variation in intercepts between twin pair means (level-two), and e_{ij} is the individual-specific random effects representing variation among individuals within twin pairs (level-one, within pair residual). Thus, the value of the dependent variable is the sum of a general mean (β_0), one or more fixed effects ($\beta_{1\text{-}N}$), a random effect at the group (twin pair) level (u_j), and a random effect at the individual level (e_{ij}). The total variance of Y_{ij} can be decomposed as the sum of the level-one (individual) and level-two (twin pair) variances (32).

Because we were interested in examining the effects of an additional fixed factor (*APOE* genotype [ε4+, ε4−]), correcting error estimates for the effect of the level two (twin pair) grouping factor, a model that estimates the effects of both fixed factors (*APOE* and recall condition [immediate, delayed]) in the presence of a random factor (twin pair) was required. *APOE* status is a fixed between-subjects factor because finite “levels” of the variable can change only between subjects. Recall condition is a repeated factor because each subject has a measurement at each level of the independent variable; it is also treated as a “fixed” factor because we were interested only in the two levels (immediate, delayed) that were measured. In addition to main effects, we tested the *APOE* status x recall condition interaction. This interaction addressed the question of differences in forgetting over time. However, none of the interactions were significant, and separate results for immediate and delayed recalled conditions were essentially the same (i.e., results that were significant for one were significant for the other). Consistent with the recommendations of Fitzmaurice et al. (33), we, therefore, simplified the results by presenting only the results for the immediate-delayed composite scores. For descriptive purposes, separate means and SDs are shown for both the immediate and delayed conditions of each measure. Cognitive asymmetry scores were computed by converting logical memory and visual reproduction scores into *z*-scores, and subtracting one *z*-score from the other. All tests were two-tailed.

It is possible that there were also variance differences as a function of zygosity or genotype concordance/discordance status. Therefore, we also performed sets of separate analyses in which the models included these different strata. These analyses are not presented because results were essentially the same as in the analyses referred to in the previous paragraph. The only differences were that with discordant pairs only, the logical memory difference was significant only at a trend level ($p<.08$) and the asymmetry score difference was not significant. Analyses that included interaction terms, zygosity, or concordance/discordance strata in the models are available from the authors. Finally, as a check on possible violation of the assumptions of the mixed models caused by the omission of these factors from the models presented, we performed analyses on a subsample comprising one randomly selected twin per pair so that all individuals would be independent observations.

Results

Table 1 shows comparisons of the ε4− and ε4+ groups on a number of demographic and clinical variables. Two significant differences emerged. The mean induction AFQT percentile score for the ε4+ group was significantly higher than that of the ε4− group. Note that because individuals scoring below the 10th percentile were excluded from military service, the mean AFQT score in VET Registry twins was above the 50th percentile. The standard deviation (SD) in VET Registry twins was about 23.5. This would mean that the overall mean AFQT score of 61.7 for the current 626 participants was about .5 SD above the population mean. This would be similar to a Wechsler (34) IQ of 107.5, which is slightly above the IQ mean of 100 (SD=15). Given the difference we observed in age 20 AFQT scores, we performed analyses with AFQT score as a covariate. The groups did not differ on the CES-D, but ratings on the item, "I worry about my memory," were significantly lower (indicating greater concern) in the ε4+ group than in ε4− group.

Tables 2 through 4 show the results of the mixed model regressions for the composite memory scores. As shown in Table 2, having at least one *APOE*-ε4 allele was associated with poorer performance on logical memories, and this effect was enhanced after adjusting for age 20 AFQT scores. Table 3 shows that performance on visual reproductions was not significantly different in the ε4+ and ε4− groups.

Table 4 presents the results of the cognitive asymmetry analyses. The groups did not differ on the absolute asymmetry scores; therefore, results shown in Table 4 are for directional (verbal minus visuospatial memory) differences only. The mean difference scores for the ε4+ group were negative and significantly larger than the difference scores for the ε4− group. This pattern indicates worse verbal relative to visuospatial memory in ε4+ compared with ε4− individuals.

Results for the analyses of the subsample comprising one twin per pair were essentially the same as the results presented in Tables 2–4. The ε4+ group had significantly better logical memory scores than the ε4− group ($F=6.34$, $p<.02$). The ε4+ group had negative asymmetry scores, whereas the ε4− group had positive asymmetry scores ($F=6.29$, $p<.02$). As in the full sample results, the groups did not differ on visual reproductions ($F=0.42$, $p=.52$).

Discussion

We observed a significant association between *APOE* genotype and cognitive performance in the same individuals at an average age of 20 and 55. *APOE*-ε4 carriers had significantly higher general cognitive ability scores at age 20 than non-carriers, but ε4 carriers had significantly poorer verbal episodic memory at age 55. Interestingly, these groups did not differ in their years of educational attainment. The highest level of educational attainment for many individuals would have been reached after the age 20 AFQT was administered, but it was long before the current assessment when they were in their 50s. Education is often used as a proxy for prior general intellectual ability because it is generally fully attained well before the late-onset disorders such as dementia. Moreover, actual prior scores are virtually never available, thus making it necessary to estimate prior cognitive ability. As would be expected, educational attainment and AFQT score were significantly correlated ($r=0.29$, $p<.001$). However, a cognitive test score such as the AFQT is a far more precise index than years of education; there will still be a good deal of variability in cognitive test scores, for example, even in individuals who have completed 12 years of education. Had we used education, we would have assumed that the ε4+ and ε4− groups were better matched than they actually were. The availability of these prior scores is a unique feature of the VETSA.

Because the ε4+ had higher age 20 AFQT scores than the ε4− group, adjusting for prior cognitive ability strengthened the significance of the group differences in memory.

It is unclear why the ε4+ group would have higher age 20 cognitive scores. Two previous studies of younger participants did not find significant differences (8, 9), and one of these studies found an effect size (not significant) in 11 year old boys of .22 such that ε4+ individuals had lower scores. In our larger sample, there was a significant effect size of .25, but with the advantage for the ε4+ group. Differences across the studies could be due to the different tests used, the different ages at testing, or chance. Although perhaps unlikely, it is nevertheless possible that this pattern might indicate the phenomenon of antagonistic pleiotropy (35), the notion that a gene may confer some beneficial effect at an earlier period of life but then have deleterious effect in older age.

In contrast to prior general cognitive ability differences, at age 55 episodic memory scores were significantly lower in ε4+ individuals than in ε4− individuals, a result that was strengthened after adjusting for prior cognitive ability. These data are consistent with cross-sectional studies that show poorer performance in learning and memory among older adults who possess at least one *APOE*-ε4 allele. To our knowledge, this is only the second study of APOE in adults under 60 years of age.

Visuospatial episodic memory did not differ as a function of APOE genotype in our midlife participants, but there was evidence of a cognitive asymmetry that was partially consistent with previous findings in much older individuals (10, 11). In the older adults there were no mean differences according to *APOE* genotype, but ε4+ individuals had greater cognitive asymmetries than ε4− individuals. We found mean differences on verbal memory as well as greater verbal-visual asymmetries in the ε4+ group. In the previous asymmetry studies, the finding was one of greater asymmetries in ε4+ individuals regardless of the direction of difference; in our middle-aged participants, the difference was significant in one direction only—with verbal below visual memory performance in the ε4+ group. The asymmetry effect was small, but asymmetries might show proportionately large increases with increasing age in *APOE*-ε4 carriers. It should also be noted that our tests were not the ideal probes for cognitive asymmetry because logical memory is strongly lateralized to the left hemisphere, but visual reproductions is not as strongly lateralized to the right hemisphere (36).

There were 24 African-American participants in the VETSA, of whom 11 (45.8%) has at least one ε4 allele. There were 598 Caucasian participants of whom 178 (29.8%) had at least one ε4 allele. There were 2 Hispanic and 2 “other” participants with no ε4 alleles. Some other samples of American Caucasians have found prevalence rates of 25.9% (37) and 27.7% (38), very similar to the rates in our sample. Our finding of elevated rates of the ε4 allele in African-Americans is also consistent with previous findings; for example, the rate among African-Americans in the Atherosclerosis Risk in Communities Study was 41.2%. Given the sample demographic characteristics, we note our results may not generalize to ethnic minorities or women. However, we can conclude that our results were not driven by the elevated proportion of ε4+ participants among African-Americans because the memory differences remained significant in analyses that were performed with African-American participants excluded (results available upon request).

Because the sample includes correlated observations (twins within pairs), it is also possible that the results could be misleading due to an imperfect accounting of all of the effects in the mixed models. The results remained consistent when zygosity or APOE concordance status was included in the models (available from authors). However, the strongest evidence against this being a cause for concern comes from the consistency of the results from the

subsample of one randomly selected twin per pair. Because individuals in the latter analysis are all independent observations, there are no strata of correlated effects that could affect the results.

None of the participants in our study were demented and none showed any indication of being in a preclinical dementia stage. Yet, there was still evidence of verbal memory deficits that were associated with the ε4 allele. The significantly greater concerns about memory suggest that although they are not demented, those individuals who possess an ε4 allele may be starting to become cognizant of subtle memory difficulties. The fact that the ε4+ and ε4− groups did not differ on depressive symptoms and that participants were unaware of their APOE genotype adds support to the idea that the expressed concerns are indicative of objective memory deficits. Such concerns have in some cases been predictive of cognitive decline (13), but our data suggest that those concerns may be meaningful even as early as the mid-50s.

Rather than adjusting for age, our findings provide direct support in a large middle-aged sample for the notion that having at least one *APOE*-ε4 allele is associated with memory deficits at least as early as the sixth decade of life, and before the prodromal stages of dementia. These results strengthen the argument that the *APOE*-genotype affects cognition in healthy aging (1). At the same time, it must be noted that the effects at this age were small; effect sizes were small by Cohen's (39) convention (.20s) for verbal memory, verbal-visual memory differences, as well as expressed concerns about memory. The VETSA project is currently in wave 1 of data collection. In future waves of the study, it will be important to examine the risk and protective factors for further cognitive decline in ε4+ carriers.

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Table 1

Demographic and clinical characteristics by APOE genotype

Characteristic	*APOE*-ε4−			*APOE*-ε4+				
	Mean	**SD**	**n**	**Mean**	**SD**	**n**	**F**	***p* Value**
Age	55.12	2.26	437	55.03	2.18	189	0.88	0.349
Current AFQT[a]	63.96	20.59	437	66.13	20.16	189	1.48	0.23
Pre-Induction AFQT[b]	60.03	22.12	437	65.51	21.54	188	8.18	0.004
Education (years)	13.79	1.99	418	13.99	2.21	175	1.11	0.29
Household Income[c]	5.98	2.93	435	5.69	2.85	189	1.33	0.25
Worry about memory[d]	3.23	0.88	401	3.04	0.94	180	5.37	0.02
Depressive symptomsf[e]	8.43	8.31	418	8.65	8.74	175	0.16	0.72

[a] Armed Forced Qualification Test percentile scores.

[b] Pre-induction refers to induction into the military.

[c] 1(<$10K) to 13 ($120K+); 6 ($50K-$59,999).

[d] 1 (definitely true) to 5 (definitely false).

[e] Means and SDs shown are for untransformed scores on the Center for Epidemiologic Studies Depression Scale (CES-D), but the statistical results are based on log-transformed scores.

Table 2

Mixed model analysis of logical memory scores by APOE genotype (ε4+ vs. ε4−) adjusted for age 20 AFQT score[a]

***APOE* group**	**ε4+**			**ε4−**		
	Mean[b]	**SD**	**n**	**Mean[b]**	**SD**	**n**
Immediate recall	22.19	5.37	186	23.78	6.20	436
Delayed recall	19.50	5.86	185	20.12	6.63	436
Immediate-delayed composite recall	20.66	5.33	185	22.01	6.18	436

Source	*df*	F	*p* Value
Intercept	1, 617	575.42	<0.001
Immediate-delayed recall composite	1, 617	6.79	0.009

[a] AFQT=Armed Forces Qualification Test

[b] Values shown are maximum likelihood estimates of marginal means adjusted for AFQT score.

Table 3

Mixed model analysis of visual reproduction scores by APOE genotype (ε4+ vs. ε4−) adjusted for age 20 AFQT score[a]

***APOE* group**	**ε4+**			**ε4−**				
	Mean[b]	**SD**	**n**	**Mean[b]**	**SD**	**n**		
Immediate recall	78.45	12.10	189	78.79	12.14	437		
Delayed recall	58.09	20.16	189	56.41	19.62	437		
Immediate-delayed composite recall	67.87	14.17	189	67.6	14.56	437		
Source				*df*			F	*p* Value
Intercept				1, 621			1062.43	<0.001
Immediate-delayed recall composite				1, 621			0.10	0.75

[a] AFQT=Armed Forces Qualification Test

[b] Values shown are maximum likelihood estimates of marginal means adjusted for AFQT score.

Table 4

Mixed model analysis of cognitive asymmetry scores by APOE genotype (ε4+ vs. ε4−) adjusted for age 20 AFQT score[a]

***APOE* group**	**ε4+**			**ε4−**				
	Mean[b]	**SD**	**n**	**Mean[b]**	**SD**	**n**		
Immediate recall	−0.24	1.07	186	0.02	1.24	436		
Delayed recall	−0.19	0.99	185	0.03	1.11	436		
Immediate-delayed composite recall	−0.22	0.97	185	0.02	1.14	436		
Source			*df*				F	*p* Value
Intercept			1, 619				5.15	0.03
Immediate-delayed recall composite			1, 619				6.29	0.01

[a] AFQT=Armed Forces Qualification Test. Cognitive asymmetry scores are the differences between standardized (z-scored) logical memory and standardized visual reproductions scores. Zero values indicate no asymmetry; positive values indicate better verbal than visuospatial memory.

[b] Values shown are maximum likelihood estimates of marginal means adjusted for AFQT score.