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Independent Effects of Apolipoprotein E and Cerebrovascular Burden on Later-Life Depression: The Wisconsin Longitudinal Study

Rosanna G. Scott, MS,[a,*] and Daniel L. Paulson, PhD[a]

ABSTRACT

Objective: Studies evaluating the effect of apolipoprotein E (*APOE*) on vascular depression are sparse, employ heterogeneous methods, and yield inconsistent results. One possibility is that *APOE* is a moderator of another predictor such as cerebrovascular burden. This longitudinal study examines the relationships between *APOE*, cerebrovascular burden, and depressive symptomatology in a large cohort sample from midlife to later life.

Methods: Data include 3,203 participants across 18 years (1993–2011) from the Wisconsin Longitudinal Study (baseline mean age = 53 years). Depressive symptomatology was measured using the Center for Epidemiologic Studies Depression scale. Cerebrovascular burden was operationalized as hypertension, high blood sugar or diabetes, and other heart problems. *APOE* genotyping was completed using saliva samples. Hypotheses were examined via a moderated path model and binary logistic regression.

Results: Results supported the hypothesized path model (root mean square error of approximation = 0.041; comparative fit index = 0.959); however, *APOE*-conferred risk was not a significant moderator of the 2004 or 2011 vascular depression effect and only approached significance as a predictor of depression in 2011 ($P = .079$). The logistic regression yielded *APOE* as a significant predictor of clinically significant depressive symptoms in 2011 ($P = .02$, Exp(B) = 1.197).

Conclusions: The present findings suggest that *APOE* may influence expression of depressive symptomatology as adults age into and beyond their mid-70s but do not indicate *APOE* as a moderator of vascular depression. Results posit a potential explanation for inconsistent past findings.

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Later-life depression is commonly undetected, despite recognition as the second leading cause of disability worldwide, associated functional impairment, and ominous health implications.[1–3] Effects of depression in later life are exacerbated by comorbid cerebrovascular burden (CVB).[4] The population of adults in the United States over 65 years of age surpasses 44 million[5] and is projected to reach 82.3 million, or 21.7% of the US population,[6] by 2040. This surge in older adults has led to increased scrutiny of effective strategies to predict, prevent, and treat disease processes. One avenue by which researchers are examining how best to provide health care to older adults is by way of genetic sequencing, which has become more affordable. Strong emphasis has been placed on relating genetic diatheses to environmental and behavioral stressors on the development of life-limiting syndromes, allowing for efficient, economical, and effective individualized medicine.[7]

Meta-analytic findings have identified apolipoprotein E (*APOE*) as a strongly implicated gene in adverse later-life health outcomes, including major depressive disorder (MDD).[8] *APOE* was first recognized for its implications in lipoprotein metabolism and cardiovascular disease and has since become known for its role in cognitive function, immunoregulation, and Alzheimer's disease (AD).[9] Each individual carries 2 copies of the *APOE* gene, 1 from each parent. There are 3 common alleles at the *APOE* locus: ε2, ε3, and ε4.[10] Thus, 6 combinations of *APOE* carriage exist that, when displayed on a continuum, reflect a dimension of *APOE*-conferred risk. Allelic frequencies of *APOE* in white samples are approximately 7% ε2, 77% ε3, and 16% ε4, with corresponding genotypic frequencies of 0.5% ε2/ε2, 11% ε2/ε3, 59% ε3/ε3, 2% ε2/ε4, 25% ε3/ε4, and 3% ε4/ε4.[10] A review of the literature indicates ε3 as most common in frequency and concomitant to normal functioning; ε2 and ε4 are scarcer and have varied functional implications.[9]

APOE is more prominently recognized in relation to the development of AD. Extant research suggests a dose-dependent effect of *APOE* isoforms on amyloid β peptide clearance, aggregation, and deposition.[11] When comparisons across isoforms are made, the presence of *APOE*4* puts individuals at significantly higher risk for developing AD (ε2/ε4, odds ratio [OR] = 2.6; ε3/ε4, OR = 3.2; ε4/ε4, OR = 14.9).[12] *APOE* has also been linked to earlier AD onset, such that individuals with the ε4/ε4 genotype have a mean age at AD onset of 66.4 years compared to all other *APOE* configurations, whose average AD age at onset is 71.3–73.6 years.[13] Similar effects of *APOE*4* on hastened disease development have been indicated in Parkinson's disease and Wilson disease.[14,15] By contrast, ε2 has been shown to reduce risk of developing AD (OR = 0.6).[12,16]

Given that *APOE* impacts the manifestation of various neurologic diseases, it is logical to presume that a similar effect exists by which *APOE* affects the pathophysiology of depression in later-life. Concurrent with this hypothesis, extant depression literature reflects substantive parallels with AD literature. López-León and colleagues[8] found that individuals possessing an *APOE*2* allele, compared to the ε3 allele, had an odds ratio of 0.51 for developing

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Clinical Points

- The impact of apolipoprotein E (*APOE*) on depression has been inconsistently reported, and research suggests that there may be interplay between cerebrovascular risk factors like diabetes and *APOE* genotype on depression.
- Those with higher *APOE*-conferred risk may be more likely to develop depressive symptoms in and beyond their 70s. While these findings do not suggest that *APOE* is a "depression gene" per se, clinicians should be aware of this increased risk.

MDD; this effect mimics the protective effect apparent with *APOE*2* and AD. Studies have also demonstrated the detrimental effect of *APOE*4*, whereby *APOE*4* carriers exhibited a significantly higher risk of increased depressive symptomatology in older age (OR = 1.75–6.10).[17,18] Further, the mean age at depression onset for *APOE*4* carriers has been shown to be significantly lower than that for noncarriers (51.4 ± 20.7 and 58.8 ± 16.8 years, respectively).[19] Although results suggesting a link between *APOE* and depression are compelling, other studies suggest no apparent effect. For example, in a study of over 17,500 individuals aged 41 to 80 years (mean = 60.9 years), there was no difference in MDD prevalence across *APOE* genotypes.[20]

CVB, Depression, and *APOE*: A Potential Intersection

The strongly supported relationship between CVB and depression in later life (for review, see references 4, 21, and 22), in conjunction with the effect of *APOE* genotype on lipoprotein metabolism and cardiovascular disease, suggests an intersection of these constructs. Research examining the relationship between CVB, *APOE*, and depression has been sparse. Some studies yield *APOE* as a significant moderator of the positive predictive effect of CVB on depressive symptomatology in older adults.[23,24] Not only have *APOE*4* carriers with comorbid CVB been shown to have greater depressive symptomatology, but they also may experience a greater number of depressive episodes and have a lower age at depression onset compared to noncarriers.[23] However, findings by Lavretsky et al[23] and Nebes et al[24] were generated from small sample sizes (16 and 92 participants, respectively), limiting interpretation of results.

Longitudinal relationships addressing the relationship between *APOE*, CVB, and later-life depressive symptomatology are relatively few among the literature. Support for a triadic relationship is dispersed across studies, although no study integrates these variables into a single, coherent theoretical or empirical model with an adequately sized and aged sample. A sufficient evaluation of *APOE*, CVB, and depressive symptomatology as it relates to aging requires a large sample of adults over 65 years and a longitudinal approach. The present study is the first to our knowledge to examine how *APOE* carriage moderates the relationship between cerebrovascular health and depressive symptomatology longitudinally from midlife to later life.

METHODS

Participants

This study utilizes data collected through the Wisconsin Longitudinal Study (WLS). The WLS is a longitudinal cohort study that includes over 10,000 randomly selected representatives of the 1957 high school graduating class from Wisconsin.[25] Data relevant to this study are from the 1993, 2004, and 2011 waves. For more information on the WLS, see Herd et al.[25]

Measures

Demographic variables. Age, sex, and income were self-reported by the participant. Education was assessed as self-reported years of formal schooling.

Cerebrovascular health variables. Medical variables used in this study were collected by self-report. Participants were asked, "Has a doctor ever told you that you have..." high blood pressure or hypertension; high blood sugar; diabetes; heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems; stroke. In this study, these comorbidities were grouped into 3 categories by organ system. Presence of hypertension was identified by endorsement of high blood pressure or hypertension. Presence of blood sugar dysregulation was identified by endorsement of high blood sugar or diabetes. Presence of cardiac disease was identified by endorsement of heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems. Participants endorsing a history of stroke were excluded; these individuals have been shown to be more likely to experience subsequent mood dysregulation.[26]

Total CVB. Total CVB is a continuous measure of cerebrovascular risk factors, comprising a participant's scores on the hypertension, high blood sugar/diabetes, and heart disease measures, emitting a total score from 0 to 3.

Genetic variable: apolipoprotein E. Saliva samples were collected from participants in 2006–2007 using Oragene kits and a mail-back protocol.[25] DNA genotyping was performed by KBioscience in Hoddesdon, United Kingdom, using homogeneous fluorescent resonance energy transfer technology coupled to competitive allele-specific polymerase chain reaction.[27] This study operationalized *APOE* continuously (as a measure of *APOE*-conferred risk, ε2/ε2 reflecting least risk, ε4/ε4 reflecting most risk) and dichotomously (presence/absence of *APOE*4*). The continuous *APOE*-conferred risk variable accounts for a dose effect of *APOE*4* as well as reported protective effects of *APOE*2*.[8]

Outcome variable: depression. Depression was measured using the Center for Epidemiologic Studies Depression scale (CES-D).[28] The CES-D is a self-reported measure of depressive symptoms experienced in the past week, with a suggested cutoff score of 16 for probable depression.[29] The internal consistency of the CES-D is high for older adults (coefficient α of 0.85 to 0.90), as is the validity of the measure.[30] This measure was utilized as a continuous degree

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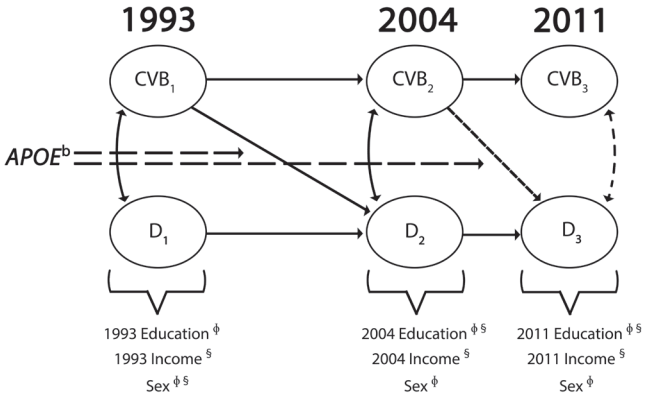
Table 1. Description of Characteristics of Sample (N = 3,203)

Variable	1993 Mean (SD)	2004 Mean (SD)	2011 Mean (SD)
Age, y	53.17 (0.61)	64.28 (0.66)	71.08 (0.86)
Education, y	13.97 (2.42)	13.99 (2.44)	13.99 (2.44)
CES-D	11.61 (7.03)	10.05 (5.96)	10.78 (6.52)
CVB (range, 0–3)	0.25 (0.49)	0.69 (0.77)	1.03 (0.88)
Household income, $[a]	59,230 (49,555)	53,144 (55,440)	35,108 (35,653)
			%
Female			53.5
Married			75.7
Race			
White			98.6
Black			0.1
Other race or refused to answer			1.3
APOE carriage			
ε2/ε2			0.4
ε2/ε3			12.6
ε2/ε4			2.0
ε3/ε3			60.0
ε3/ε4			23.0
ε4/ε4			2.0

[a]Household income is represented by median and interquartile range.
Abbreviations: *APOE* = apolipoprotein E, CES-D = Center for Epidemiologic Studies Depression scale, CVB = cerebrovascular burden.

Figure 1. The Relationship Between CVB and Depressive Symptomatology, and the Moderating Effect of Apolipoprotein E (*APOE*) on That Relationship, From Midlife to Later Life[a]



[a]Root mean square error of approximation = 0.041; comparative fit index = 0.959.
[b]*APOE*-conferred risk.
§Denotes a significant relationship between the control variable and depressive symptomatology.
ϕDenotes a significant relationship between the control variable and CVB.
—Denotes $P < .05$.
- - -Denotes marginal significance.
– –Denotes a nonsignificant relationship.
Abbreviations: CVB = cerebrovascular burden, D = depressive symptomatology.

of depressive symptomatology in the moderated path model and a dichotomized measure of clinically significant depressive symptoms in the logistic regression (< 16/≥ 16).

Statistical Methodology

To evaluate the validity of the *APOE* data, a correlational analysis was employed relative to measures of delayed word recall in 2011, as *APOE*4* carriers have been shown to exhibit greater decline in semantic memory ability compared to non-E4 carriers.[31,32] To model the effect of *APOE* on the relationship between CVB and depressive symptomatology over time, a moderated path model was employed. This model includes autoregressive pathways to demonstrate, for example, the effect of 1993 CVB on 2004 CVB. This model also includes cross-lagged pathways representing the hypothesized causal effect of CVB on depressive symptomatology over time. Interaction terms representing the effect of *APOE* on the relationship between CVB and depressive symptomatology in 2004 and 2011 were included. Full information maximum likelihood estimation (FIML) was utilized to prevent listwise deletion to avoid the underrepresentation of at-risk respondents on variables associated with mortality-based attrition (eg, socially marginalized individuals with limited health care access, or those carrying greater medical burden). On the basis of past studies, sex, education, and income were set as control variables. For the moderated path analysis, *APOE* was analyzed continuously and dichotomously. Logistic regression was employed to assess the cross-sectional relationship of *APOE*-conferred risk, CVB, and their interaction on clinically significant depressive symptoms in 1993, 2004, and 2011; sex, income, education, and marital status were included as control variables. Data were prepared in SPSS Version 23; the structural equation model analysis was performed utilizing the Mplus software program.[33]

RESULTS

The final sample consisted of 3,203 participants. See Table 1 for participant characteristics. Mean participant age was 53 years in 1993, 64 years in 2004, and 71 years in 2011. Within the moderated path model, the largest proportion of missing data was depressive symptomatology; 6.6%, 11.4%, and 17.2% of participants' depressive symptomatology data were estimated using FIML in 1993, 2004, and 2011, respectively. Only 0.6% of participants' CVB data were missing in 2011. A correlational analysis was conducted to evaluate the relationship between *APOE*-conferred risk and delayed word recall in 2011. Results yielded a significant negative correlation between *APOE*-conferred risk and performance on a delayed word recall task ($r = -0.081$, $P = .01$).

The longitudinal effect of *APOE*-conferred risk on the relationship between CVB and depressive symptomatology was modeled by a moderated path analysis. Overall, results suggest that the hypothesized model fit the data very well (root mean square error of approximation = 0.041; comparative fit index = 0.959; Figure 1). With respect to the model's autoregressive pathways that evaluated the relationship between previous and future CVB, greater CVB in 1993 significantly predicted greater CVB in 2004 ($\beta = 0.498$, SE = 0.013, $P < .001$). Further, greater CVB

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Table 2. Longitudinal Relationships on Depressive Symptomatology (N = 3,203)[a]

	1993 β (SE)	2004 β (SE)	2011 β (SE)
Education	−0.010 (0.019)	−0.036 (0.016)*	−0.039 (0.016)*
Income	−0.127 (0.019)**	−0.040 (0.017)*	−0.043 (0.017)*
Sex	0.095 (0.018)**	0.030 (0.016)	0.009 (0.016)
APOE	…	0.008 (0.016)	0.028 (0.016)
1993 CVB	…	0.037 (0.016)*	…
1993 CVB × *APOE*	…	0.007 (0.016)	…
2004 CVB	…	…	0.030 (0.016)
2004 CVB × *APOE*	…	…	0.000 (0.016)

[a]All autoregressive pathways for CVB and depression were significant.
*$P < .05$.
**$P < .001$.
Abbreviations: *APOE* = apolipoprotein E, CVB = cerebrovascular burden.
Symbol: … = not applicable

in 2004 was significantly associated with greater CVB in 2011 (β = 0.694, SE = 0.009, $P < .001$). The autoregressive pathways that demonstrated the relationship between prior and future depressive symptomatology revealed a similar relationship whereby higher CES-D scores in 1993 were significantly associated with higher CES-D scores in 2004 (β = 0.548, SE = 0.013, $P < .001$), and higher CES-D scores in 2004 were significantly related to higher CES-D scores in 2011 (β = 0.594, SE = 0.013, $P < .001$). With respect to the cross-lagged pathways that identified the relationship between CVB and depressive symptomatology from previous waves to future waves, greater CVB in 1993 was significantly associated with higher CES-D scores in 2004 (β = 0.037, SE = 0.016, $P = .018$). Greater CVB in 2004 was a marginally significant predictor of higher CES-D scores in 2011 (β = 0.030, SE = 0.016, $P = .067$). There was no significant main effect of *APOE*-conferred risk on depressive symptomatology in 2004; however, this relationship approached significance in 2011 (β = 0.028, SE = 0.016, $P = .079$).

The interaction between *APOE*-conferred risk and CVB was not significant with respect to depressive symptomatology in 2004 or 2011, indicating that *APOE* does not moderate the demonstrated vascular depression effect. Overall, the model accounted for 37.1% of the 2011 depressive symptomatology variance.

All control variables had statistically significant pathways dependent upon the wave. Education was significantly inversely related to CVB in 1993, 2004, and 2011. Education was also significantly inversely related to depressive symptomatology in 2004 and 2011. Income was significantly inversely associated with depressive symptomatology in 1993, 2004, and 2011. Male sex was significantly associated with higher CVB in 1993, 2004, and 2011. Lastly, female sex was significantly predictive of depressive symptomatology in 1993 and was marginally significantly predictive of depressive symptomatology in 2004. See Table 2 for the pathway coefficients for the moderated path analysis.

To maintain consistency with extant *APOE* research, the moderated path model was also run using an *APOE* variable dichotomized for presence or absence of an *APOE*4* allele. Results were similar to those of the initial analysis. *APOE*4* carriage was not significantly predictive of depressive symptomatology in 2004 (β = 0.008, SE = 0.016, $P = .589$) or 2011 (β = 0.015, SE = 0.016, $P = .344$). Further, *APOE*4* carriage did not significantly moderate the relationship between CVB and depressive symptomatology in 2004 (β = 0.002, SE = 0.015, $P = .913$) or 2011 (β = −0.018, SE = 0.016, $P = .27$).

To evaluate the cross-sectional relationship of *APOE*-conferred risk, CVB, and their interaction on clinically significant depressive symptoms in 1993, 2004, and 2011, binary logistic regressions using simultaneous entry were employed. In regard to clinically significant depressive symptoms in 2011, control variables were entered into the analysis in block 1, resulting in a significant model (χ^2 [4, N = 2,958] = 79.542, $P < .001$, Nagelkerke $R^2 = .045$). In block 2, *APOE*-conferred risk and 2011 CVB were added into the analysis, contributing significantly to the model (χ^2 [2, N = 2,958] = 26.476, $P < .001$), and the model remained significant (χ^2 [6, N = 2,958] = 106.018, $P < .001$, Nagelkerke $R^2 = .059$). *APOE*-conferred risk significantly predicted clinically significant depressive symptoms (β = 0.180, SE = 0.077, $P = .02$, Exp(B) = 1.197), as did 2011 CVB (β = 0.262, SE = 0.057, $P < .001$, Exp(B) = 1.300). In block 3, the interaction between *APOE*-conferred risk and 2011 CVB was added into the analysis; however, this did not significantly contribute to the model (χ^2 [1, N = 2,958] = 0.298, $P = .585$). In block 3, the significant main effects of *APOE*-conferred risk and 2011 CVB on clinically significant depressive symptoms remained; their interaction was not significant. See Table 3 for the 2011 binary logistic regression results. The logistic regressions for *APOE*, CVB, and their interaction on clinically significant depressive symptoms in 2004 and 1993 yielded similar results; however, *APOE* was not a significant predictor of clinically significant depressive symptoms in 2004 or 1993 ($P = .285$ and $P = .82$ in block 2, respectively), nor was its interaction with CVB.

DISCUSSION

Present findings suggest that *APOE* is implicated in the predisposition and perpetuation of later-life depressive symptomatology, particularly as adults age into and beyond their 70s. CVB also predicted later-life depressive symptomatology, a finding that is consistent with the extensively studied vascular depression hypothesis.[4,21,22] However, results do not suggest that *APOE* moderates the vascular depression effect. Within the context of inconsistent literature on the impact of *APOE* on depressive symptomatology, our findings support a relationship between *APOE* and depressive symptomatology that is independent of CVB and that may not become evident until later life.

In the longitudinal analysis, *APOE*-conferred risk did not significantly predict depressive symptomatology at age 64 years, although this relationship approached significance when participants were 71 years ($P = .079$). The

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Table 3. Logistic Regression of CVB, *APOE*, and Their Interaction on Clinically Significant Symptoms of Depression in 2011 (N = 2,958)

	Block 1		Block 2			Block 3	
	β (SE)	Wald	β (SE)	Wald	Exp(B)[b]	β (SE)	Wald
Sex	0.219 (0.106)	4.275*	0.302 (0.108)	7.793**	1.352	0.301 (0.108)	7.765**
Income	–0.165 (0.040)	16.601***	–0.153 (0.041)	14.159***	0.858	–0.154 (0.041)	14.260***
Education	–0.088 (0.023)	14.409***	–0.079 (0.024)	11.262***	0.924	–0.078 (0.024)	11.093***
Marital status	–0.358 (0.113)	10.059**	–0.377 (0.114)	11.006***	0.686	–0.375 (0.114)	10.866***
CVB	…	…	0.262 (0.057)	21.048***	1.300	0.260 (0.057)	20.639***
APOE[a]	…	…	0.180 (0.077)	5.448*	1.197	0.176 (0.077)	5.194*
CVB × *APOE*[a]	…	…	…	…	…	0.047 (0.087)	0.298
Constant	0.048 (0.389)	0.015	–0.248 (0.396)	0.390	0.781	–0.254 (0.397)	0.409

[a]*APOE*-conferred risk.
[b]Exp(B) displayed for the most parsimonious model.
*$P < .05$.
**$P \leq .01$.
***$P \leq .001$.
Abbreviations: *APOE* = apolipoprotein E, CVB = cerebrovascular burden.
Symbol: … = not applicable.

cross-sectional analysis of *APOE*-conferred risk on clinically significant depressive symptoms yielded a significant relationship for participants at age 71 years; this relationship was weakened in 2004 ($P = .285$) and even more so in 1993 ($P = .82$). The moderated path model more appropriately accounts for missing data in this population and also considers the effect of prior depressive symptomatology on future depressive symptoms, thus weakening the relationship between *APOE*-conferred risk and depressive symptomatology to marginal significance. Taken together, however, these results suggest that *APOE* is implicated in depressive symptomatology as adults approach and surpass their mid-70s.

This hypothesis fits well within the context of past research. Surtees and colleagues,[20] with a substantially powered sample size, found no relationship between *APOE* and MDD in adults with a mean age of 60.9 years. Meanwhile a recent 9-year follow-up study by Skoog et al[18] *did* yield a significant relationship between *APOE*4* and the incidence of depression in a sample whose mean age was about 74 years at baseline. Further, Steffens and colleagues[34] found an increased effect of *APOE*4* on late-onset depression in adults over 80 years compared to those younger than 80 years. In sum, the aggregate of past and present research on the impact of *APOE* on depressive symptomatology supports a significant relationship that develops in the mid-to-late 70s.

Given the moderate relationship between *APOE*-conferred risk and depressive symptomatology within the context of myriad psychosocial variables associated with depressive symptoms, the present findings should be interpreted in light of their clinical significance. With respect to the 2011 logistic regression, a 1-unit increase in *APOE*-conferred risk increased the odds of a 71-year-old meeting the CES-D clinical cutoff for probable depression by 19.7%. Although the relationship between *APOE*-conferred risk and depressive symptomatology in 2011 was not significant in the moderated path model ($P = .079$), the standardized results of this relationship indicate that for each standard deviation increase in *APOE*-conferred risk, there is an increase of 0.028 standard deviation in depressive symptomatology. Despite these statistical results, the clinical significance of these findings does not indicate *APOE* as a "depression gene" and does not implicate *APOE* as a primary target for depression intervention. Nonetheless, results of the present study address the role of *APOE* in depressive symptomatology as adults age, a relationship that has been heterogeneously assessed and inconsistently reported in the literature. This study also examines *APOE* as a moderator of the vascular depression effect, a hypothesis of sound theoretical rationale and which has been preliminarily supported by studies that are admittedly underpowered.[23,24] In the absence of common methodological barriers, *APOE*-conferred risk did not significantly moderate the vascular depression effect.

The primary limitation of this study is the use of a racially homogeneous, well-educated sample. The effect of *APOE* on various neurologic diseases such as AD has been shown to fluctuate between ethnic groups.[35] Future research should seek to replicate these findings in a sample of greater racial and socioeconomic diversity. A second limitation is the use of self-reported health data in measuring CVB. However, this approach is consistent with past research on clinically defined vascular depression, and subjective accounts of medical burden have yielded high concordance with objective measures.[36,37] A third limitation exists in the evaluation of chronological change imposed by using only 3 defined time points over an extended span of time. To our knowledge, very few datasets exist that represent such a large sample from midlife to later life, limiting the feasibility of a more ideal analysis of these interrelationships.

Future research should continue examining the impact of *APOE* on neurologic disorders, in conjunction with identifying alternative genetic risk factors for disordered health. The imminent increase in older adults makes the identification of idiographic risk factors critical for disorders more prevalent in later life. A better understanding of the diatheses by which pathology develops will inherently lead to more effective individualized treatments and subsequent improved collaboration across health care providers.

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Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Geriatric Psychiatry section. Please contact Helen Lavretsky, MD, MS, at hlavretsky@psychiatrist.com, or Gary W. Small, MD, at gsmall@psychiatrist.com.

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