



## Featured Article

## Association of midlife lipids with 20-year cognitive change: A cohort study

Melinda C. Power<sup>a,b,\*</sup>, Andreea Rawlings<sup>b</sup>, A. Richey Sharrett<sup>b</sup>, Karen Bandeen-Roche<sup>c</sup>,  
Josef Coresh<sup>b,c</sup>, Christie M. Ballantyne<sup>d</sup>, Yashashwi Pokharel<sup>d,e</sup>, Erin D. Michos<sup>b,f</sup>,  
Alan Penman<sup>g</sup>, Alvaro Alonso<sup>h</sup>, David Knopman<sup>i</sup>, Thomas H. Mosley<sup>j</sup>, Rebecca F. Gottesman<sup>b,k</sup>

<sup>a</sup>Department of Epidemiology and Biostatistics, George Washington University Milken Institute School of Public Health, Washington, DC, USA

<sup>b</sup>Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

<sup>c</sup>Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

<sup>d</sup>Department of Medicine, Baylor College of Medicine, Houston, TX, USA

<sup>e</sup>Saint Luke's Mid America Heart Institute, University of Missouri, Kansas City, MO, USA

<sup>f</sup>Department of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

<sup>g</sup>Center of Biostatistics and Bioinformatics, University of Mississippi Medical Center, Jackson, MS, USA

<sup>h</sup>Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, USA

<sup>i</sup>Department of Neurology, Mayo Clinic, Rochester, MN, USA

<sup>j</sup>Department of Medicine, University of Mississippi Medical Center, Jackson, MS, USA

<sup>k</sup>Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

**Abstract**

**Introduction:** Existing studies predominantly consider the association of late-life lipid levels and subsequent cognitive change. However, midlife rather than late-life risk factors are often most relevant to cognitive health.

**Methods:** We quantified the association between measured serum lipids in midlife and subsequent 20-year change in performance on three cognitive tests in 13,997 participants of the Atherosclerosis Risk in Communities study.

**Results:** Elevated total cholesterol, low-density lipoprotein cholesterol, and triglycerides were associated with greater 20-year decline on a test of executive function, sustained attention, and processing speed. Higher total cholesterol and triglycerides were also associated with greater 20-year decline in memory scores and a measure summarizing performance on all three tests. High-density lipoprotein cholesterol was not associated with cognitive change. Results were materially unchanged in sensitivity analyses addressing informative missingness.

Dr. Power and Dr. Mosley report grants from NIH, during conduct of the study; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; and no other relationships or activities that could appear to have influenced the submitted work. Dr. Coresh reports grants from NIH and NKF, during the conduct of the study; grants from NIH, grants from NKF, outside the submitted work; In addition, Dr. Coresh has a patent PCT/US2015/044567. Provisional patent (Coresh, Inker, and Levey) filed 8/15/2014—Precise estimation of glomerular filtration rate from multiple biomarkers issued. Dr. Gottesman reports no support from any organization for the submitted work; personal fees from *Neurology* journal, where she serves as an associate editor, outside the submitted work; and no other relationships or activities that could appear to have influenced the submitted work. Dr. Ballantyne, Dr. Sharrett, Dr. Rawlings, Dr. Alonso, Dr. Pokharel, and Dr. Penman report no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work

in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work. Dr. Michos reports no support from any organization for the submitted work; personal fees from Siemens Diagnostics, outside the submitted work; and no other relationships or activities that could appear to have influenced the submitted work. Dr. Knopman reports no support from any organization for the submitted work; personal fees from DIAN study DSMB, personal fees from Lundbeck AD drug DSMB, outside the submitted work; and no other relationships or activities that could appear to have influenced the submitted work. Dr. Bandeen-Roche reports grants from NIH, during the conduct of the study; grants from NIH, outside the submitted work; and no other relationships or activities that could appear to have influenced the submitted work.

\*Corresponding author. Tel.: +1-202-994-7778; Fax: +1-202-994-0082.

E-mail address: melindacpower@gmail.com

**Discussion:** Elevated total cholesterol, low-density lipoprotein cholesterol, and triglycerides in midlife were associated with greater 20-year cognitive decline.

© 2017 Published by Elsevier Inc. on behalf of the Alzheimer's Association.

**Keywords:** Lipids; Cognition; Dementia; Epidemiology; Cohort; Longitudinal; Cognitive decline; Cognitive change; Cholesterol

## 1. Introduction

Despite sustained interest, the impact of lipid levels on late-life cognition remains unclear. Prior studies of elevated late-life lipids and subsequent risk of incident dementia report either null results or protective associations [1,2]. Studies of elevated midlife total cholesterol and risk of dementia are mixed, with many [3–8] but not all [9,10] reporting adverse associations. Accelerated cognitive decline is also itself a concern, even if it never progresses to dementia [11]; therefore, risk factors for cognitive change represent potential targets for intervention with the dual goal of improving quality of life and preventing dementia. Associations between risk factors and cognitive change are also less susceptible to reverse causation and confounding than associations between risk factors and cognitive status. Although existing studies have examined the association between late-life lipids and near-term cognitive change [12–16], the impact of midlife or decades-prior lipid levels on cognitive change remains unknown. In addition, questions remain about the influence of contextual factors, including race and apolipoprotein (APOE)  $\epsilon$ 4 allele status. Most prior studies of lipids and cognition have examined predominately white populations. Although existing studies of midlife lipids and dementia collectively do not support a synergistic effect of APOE and lipids on dementia risk [1], there is evidence in other contexts to suggest that the combination of vascular risk factors and APOE may confer greater risk of cognitive deterioration than would be otherwise expected [17,18]. Therefore, our goal was to consider the association between multiple lipid fractions in midlife and 20-year cognitive decline using data from the large and predominantly biracial Atherosclerosis Risk in Communities (ARIC) study, overall and within selected subgroups.

## 2. Methods

### 2.1. Study population

ARIC is a longitudinal cohort study of 15,792 persons recruited at ages 45 to 65 years from four U.S. communities: Minneapolis suburbs, MN; Forsyth County, NC; Washington County, MD; and Jackson, MS [19]. All participants in Jackson, MS were black. Five study visits have been completed: visit 1 (1987–1989), visit 2 (1990–1992), visit 3 (1993–1995), visit 4 (1996–1998), and visit 5/ARIC Neurocognitive Study (visit 5/ARIC-NCS, 2011–2013). Visit 2, the time of the first cognitive testing, serves as study baseline.

For this analysis, we excluded ARIC participants who did complete cognitive testing at visit 2 ( $n = 1752$ ). We also excluded 43 individuals who were neither black nor white, were nonwhite from MD or MN, or who did not agree to use of their genetic data, to allow for adequate control of confounding by race-ethnicity and APOE  $\epsilon$ 4 status. This study was approved by the institutional review boards of all participating institutions. All subjects provided written informed consent to participate at each study visit, based on local standards.

### 2.2. Lipid measurements

We considered concentrations of total cholesterol, low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), and triglycerides, regardless of fasting status, at visit 2. Most participants (97.0%) had been fasting  $>8$  hours at the time of blood draw. Details of blood collection, handling, storage, and lipid measurement are available elsewhere [20]. Briefly, plasma total cholesterol and triglycerides were measured using enzymatic methods [21,22], whereas HDL-c concentrations were determined after precipitation of non-HDL lipoproteins [23,24]. LDL-c was calculated using the Friedewald equation for those with triglycerides  $<400$  mg/dL (4.52 mmol/L) [25]. Blind-duplicate coefficients of variation ranged from 5% to 10% [20].

### 2.3. Cognitive assessment

At visits 2, 4, and 5, trained study personnel administered three cognitive tests in a standard order in a quiet room: the Delayed Word Recall Test (DWRT) [26], the Digit-Symbol Substitution Test (DSST) [27], and the Word Fluency Test (WFT) [28].

The DWRT assesses verbal learning and memory. Participants are asked to learn 10 nouns, use them in sentences, and recall them 5 minutes later; the score is the number of correctly recalled nouns. The DSST is a test of executive function, sustained attention, and processing speed. Participants translate symbols to numbers using a key; the score is the number of correct translations within 90 seconds. The WFT is a test of phonemic fluency where participants are asked to generate words starting with a specific letter during a 60-second interval. We used the letters F, A, and S; the score is the number of correct words generated over all three trials.

All scores were roughly normally distributed. We created z-scores for each test using the mean and SD of scores at visit

Download English Version:

<https://daneshyari.com/en/article/8680016>

Download Persian Version:

<https://daneshyari.com/article/8680016>

[Daneshyari.com](https://daneshyari.com)