Response to Letter by Hadjiev and Mineva

Response:
We thank Drs Hadjiev and Mineva for their comments on our recent paper linking carotid intimal medial thickness (IMT) and cognitive decline among adults without clinical vascular disease. First, we agree that a single assessment of IMT is inadequate to assess lifetime progression of carotid atherosclerosis. However, epidemiological studies have demonstrated that a single IMT assessment is a potent cardiovascular risk factor, and other midlife risk factor levels (eg, blood pressure) are strong predictors of late-life cognitive outcomes. Furthermore, we consider IMT as a measure of subclinical vascular disease, not atherosclerosis per se and not carotid stenosis, which represents a frank clinical disease process. Also, on average, carotid IMT does progress rather than regress over time. Although we agree that smoking status could have been better characterized (as is true in many epidemiological investigations), we are confident that additional specification of this covariate would not have significantly changed our results. Because only 5.6% of our sample identified themselves as current smokers, our “ever/never” distinction is the most informative approach given available data. As Drs Hadjiev and Mineva have stated, socioeconomic status may be an important effect modifier of associations between IMT and cognitive function. Importantly, the sample in our recent publication was relatively homogenous (eg, our average participant had approximately 1 year of postundergraduate education), making it more difficult to assess the relative influences of socioeconomic status. Our sample’s socioeconomic homogeneity, regardless of race or ethnicity, also offers the advantage of limiting this source of variation. Moreover, Drs Hadjiev and Mineva cite the work of Singh-Manoux and colleagues, who identified a cross-sectional IMT—cognition association only among a lower socioeconomic status group. In contrast, our findings support a longitudinal relation among a largely higher socioeconomic status group, suggesting that significant IMT—cognition associations may be overlooked without the advantage of longitudinal data. We are presently investigating the roles of socioeconomic status and race in another study, Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS), in which we hope to reexamine the longitudinal effects we just reported in a more socioeconomically diverse sample. Lastly, and consistent with our description of proposed mechanisms in our Discussion section, Drs Hadjiev and Mineva correctly point out the possible contribution of MRI abnormalities such as silent white matter lesions to our findings. However, this possibility does not render our results inconsequential, given (1) the importance of independently examining measures of generalized macrovascular disease in addition to measures of localized microvascular disease; and (2) the relative ease of implementation and lesser cost of ultrasonography versus MRI studies. Despite relatively minor limitations, our investigation was the first of its kind to consider carotid IMT in relation to longitudinal performance on an extensive neuropsychological battery over an extended follow-up period of up to 11 years. We agree that future research combining longitudinal carotid ultrasonography, longitudinal comprehensive neuropsychological testing, and longitudinal neuroimaging will likely further illuminate the contribution of subclinical vascular disease to suboptimal brain health. Our findings establish a strong foundation on which to build such complex investigations.

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Disclosures
None.

Carrington Rice Wendell, MA
Department of Psychology
University of Maryland, Baltimore County
Baltimore, Md
National Institute on Aging
Intramural Research Program
National Institutes of Health
Baltimore, Md

E. Jeffrey Metter, MD
Samer S. Najjar, MD
National Institute on Aging
Intramural Research Program
National Institutes of Health
Baltimore, Md

Shari R. Waldein, PhD
Department of Psychology
University of Maryland, Baltimore County
Baltimore, Md, and
Division of Gerontology
Department of Medicine
University of Maryland School of Medicine & Geriatric Research Education and Clinical Center
Baltimore VA Medical Center
Baltimore, Md

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Carrington Rice Wendell, Alan B. Zonderman, E. Jeffrey Metter, Samer S. Najjar and Shari R. Waldstein

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