Antihypertensive Therapy and Cognition
More Questions Than Answers

John C.M. Brust, MD

See related article, pages 1165–1170

An article in this issue of Stroke by Peila et al., that duration of antihypertensive therapy seems to correlate with a reduced risk for both dementia and nondementing cognitive decline in elderly men, revisits a number of tantalizing questions, some of which are specifically mentioned by the authors and some not. What, pathophysiologically, is subsumed under the term “vascular dementia”? Can hypertension impair cognition by causing small vessel disease and widespread microinfarction in the absence of clinical stroke? Is such a process reflected in cerebral white matter hyperintensities on MRI? How specific are such abnormal signals for microvascular disease, and to what degree do they correlate with cognitive decline? Can hypertension damage neurons independently of vasculopathy? Does vasculopathy contribute to Alzheimer disease? Is hypertension a risk factor for Alzheimer disease or does it simply add to the cognitive decline by superimposing microvascular lesions? Might certain antihypertensive drugs protect against dementia by mechanisms other than blood pressure–lowering?

Peila et al’s 848 subjects, from the Honolulu-Heart Program/Honolulu-Asia Aging Study, had a mean age of 77 years and had been hypertensive from midlife. Some had never been treated; others had been treated, variably, from <5 years to >12 years. Dementia-free at baseline cognitive assessment, they were periodically reassessed for up to 7 years. Four hundred and forty-six normotensives served as controls. During follow-up 108 subjects became demented, 65 with Alzheimer disease, 19 with vascular dementia, and 24 with dementia from other causes.

For each year of antihypertensive treatment there was a 3% reduction in the risk for dementia, including both Alzheimer disease and vascular dementia. Treatment was also associated with reduction in cognitive decline short of dementia. As might be expected, the benefit of longer duration treatment was most evident in those whose blood pressure was well controlled. On the other hand, longer duration of treatment also produced benefit among those with “noncontrolled” blood pressure, suggesting a nonantihypertensive drug effect.

The medications used were not identified and undoubtedly varied from subject to subject and for some were changed during many years of treatment. Moreover, MRI imaging was not performed, and so whether dementia or cognitive decline was associated with white matter signals is unknown. Finally, as the authors acknowledge, definitively determining whether treating hypertension in the elderly reduces the risk of dementia or cognitive decline would require a prospective, randomized controlled trial, yet widespread agreement that antihypertensive therapy is indicated in such persons makes it unlikely that such a study can be performed.

Reference

Key WORDS: dementia ■ hypertension
Antihypertensive Therapy and Cognition: More Questions Than Answers
John C.M. Brust

Stroke. 2006;37:1146; originally published online April 6, 2006;
doi: 10.1161/01.STR.0000217638.48894.bc
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2006 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/37/5/1146

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office.
Once the online version of the published article for which permission is being requested is located, click
Request Permissions in the middle column of the Web page under Services. Further information about this
process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/