Re: Pulse Pressure and Risk of Alzheimer Disease in Persons Aged 75 Years and Older

To the Editor:

Qiu et al 1 conclude that an increased pulse pressure, which is a clinical indication of large-artery stiffness and severe atherosclerosis, may increase the risk of Alzheimer disease (AD) and dementia. In addition, lower pulse pressure may increase the risk of AD and dementia through a deleterious effect on cerebral perfusion.

Neurobiological features are suggested by: evidence linking vasospasm and dysregulation of the microvasculature with dopamine (DA) abnormalities lateralized to the right hemisphere; the association of reduction of blood pressure with longer, less recurrent speech hesitation pauses about 2 seconds linked to prefrontal cortex modulation of DA during the delayed alternation task; and optimum response organization and working memory at intermediate DA tone in a mediofrontostratal activation system. This hypothesis is supported by reports that the microvascular response to the onset of neuronal activity is delayed consistently about 3 seconds and is linked to increased coherence of electroencephalograph gamma-band activity (30 to 50 Hz or broader, centered on 40 Hz) associated with the execution of more complex tasks; and a 2.5- to 3-second delay period for inhibition shapes the temporal flow of information in the prefrontal cortex.2

These findings suggest confirming underlying mechanisms1 by evaluating DA D3 receptors, but not D1 or D4 receptors, involved in the rewarding effects of brain stimulation through attention to temporal signals highlighting significant stimuli.3 This strategy is supported by a study demonstrating that auditory training induces asymmetrical changes in cortical neural activity.4

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Stroke. 2003;34:e107; originally published online July 17, 2003;
doi: 10.1161/01.STR.0000083487.94236.3D
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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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:
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