

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

To the Editor:

Qiu et al<sup>1</sup> 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 mediofrontostriatal 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.<sup>2</sup>

These findings suggest confirming underlying mechanisms<sup>1</sup> by evaluating DA D<sub>2</sub> receptors, but not D<sub>3</sub> or D<sub>4</sub> receptors, involved in the rewarding effects of brain stimulation through attention to temporal signals highlighting significant stimuli.<sup>3</sup> This strategy is supported by a study demonstrating that auditory training induces asymmetrical changes in cortical neural activity.<sup>4</sup>

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