Plasma beta-amyloid levels associated with cognitive decline

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protein fragments associated with Alzheimer's disease when they accumulate in the brain—appear to be associated with faster cognitive decline even in those who do not develop dementia, according to a report posted online today that will appear in the December print issue of *Archives of Neurology*, one of the JAMA/Archives journals.

The amyloid cascade hypothesis suggests that Alzheimer's disease develops when the body is unable to metabolize glycoproteins, the precursors to amyloid, according to background information in the article. Beta-amyloid 40 and beta-amyloid 42 then accumulate, and this accumulation is considered the primary trigger for the development of Alzheimer's disease. Previous research suggests that plasma beta-amyloid levels decrease as brain beta-amyloid levels increase, prompting interest in whether plasma beta-amyloid level could be used as a biomarker for Alzheimer's disease.

Stephanie A. Cosentino, Ph.D., of Taub Institute for Research in Alzheimer's Disease and the Aging Brain, Columbia University Medical Center, New York, and colleagues studied 880 individuals who were free of dementia at the beginning of the study and who had at least two plasma beta-amyloid measurements approximately four and one-half years apart. Participants were assessed for cognitive change using an overall thinking, learning and memory score as well as in separate memory, language and visuospatial domains. Between the two beta-amyloid measurements, 481 participants remained cognitively healthy, 329 were cognitively or functionally impaired but did not have dementia

and 70 developed Alzheimer's disease.

High plasma beta-amyloid levels at the beginning of the study, along with decreasing or relatively stable values over time, were associated with faster cognitive declines in multiple domains. This association persisted even when only those who did not develop dementia were analyzed.

"Examination of specific cognitive domains in the current study revealed that global cognitive change in healthy elderly individuals was driven primarily by memory, rather than language or visuospatial abilities," the authors write. "This seemingly selective association with memory has several interpretations. First, it may suggest that healthy elderly people with a high-risk beta-amyloid profile are in the early stages of Alzheimer's disease but have not yet demonstrated sufficient change in non-memory domains to meet criteria for dementia."

It may also be that changes in amyloid levels are an important factor in cognitive aging, independent of the development of Alzheimer's disease, they note. "Stated differently, the observable change in both plasma beta-amyloid and memory in this group could be a fundamentally different process than that involved in Alzheimer's disease or might fall short of a critical threshold beyond which the full pathological presentation and clinical dementia syndrome of Alzheimer's disease would unfold," the authors conclude. "It is thus important for future work to determine more definitively the specificity of beta-amyloid profiles for predicting dementia vs. their significance for cognitive aging more generally."

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