Epigenetic 'age' predicts cognitive function

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Epigenetic markers of cognitive aging can predict performance on cognitive tests later in life, according to a study published in the journal *Aging*.

This epigenetic age score could be used to identify individuals at risk of

later dementia, facilitating early intervention that would otherwise not be possible, according to Lifang Hou, MD, Ph.D., chief of Cancer Epidemiology and Prevention in the Department of Preventive Medicine and senior author of the study.

"This could help individuals understand they need to modify their lifestyle and bring awareness to people with accelerated aging," said Hou, who is also director of the Center for Global Oncology, part of the Robert J. Havey, MD Institute for Global Health.

Normally, by the time a diagnosis of Alzheimer's disease or dementia is made, significant neurodegeneration has already occurred. Before that point, cognitive function questionnaires or brain imaging can reveal sub-clinical cognitive decline, but imaging is expensive and cognitive function questionnaires can produce inconsistent results.

"There is a need for easily accessed, quantitative biomarkers," said Yinan Zheng, Ph.D., assistant professor of Preventive Medicine in the Division of Cancer Epidemiology and Prevention.

Previous studies have linked specific epigenetic changes with aging and aging-related diseases, so the scientists developed an epigenetic age score to quantify the biological age. The score measures DNA methylation of specific genomic regions, which alters expression levels of several genes, including epigenetic "clock" genes and other genes related to immune function, adipocytokine signaling, lipid metabolism and inflammation.

The score is reported as an "epigenetic age," designed to interpret in comparison to one's chronological age. For example, someone with a chronological age of 50 but an epigenetic age of 60 is considered to have accelerated epigenetic aging.

The investigators applied this epigenetic age at two different time points to middle-aged participants in the Coronary Artery Risk Development in Young Adults (CARDIA) study, a long-term study of cardiovascular risk factors which began in 1983 with participants in young adulthood. The study authors also used brain imaging data to quantify "brain age" in the same participants. These two aging markers, both assessed at two time points, were associated with those same participants' performance on cognitive function tests.

Accelerated epigenetic age in midlife was predictive of cognitive performance five to ten years later. Importantly, epigenetic age and brain age were weakly correlated, underlining their complementary information relevant to accelerated cognitive aging. In fact, adding brain age information further improved the prediction accuracy of epigenetic age, according to Zheng.

"Epigenetic age is a relatively stable biomarker with strong long-term predictive performance for cognitive function, whereas a brain age biomarker may change more dynamically in temporal association with cognitive decline," Zheng said.

This epigenetic age, coupled with brain age, could be a useful early screening tool to identify patients at risk of dementia or Alzheimer's disease, but the authors cautioned that these aging markers need to be further calibrated and validated in an older cohort with clinical dementia events.

Hou and Zheng said they are actively searching for collaborators who have access to patient cohorts that fit these requirements.

More information: Yinan Zheng et al, Mid-life epigenetic age, neuroimaging brain age, and cognitive function: coronary artery risk development in young adults (CARDIA) study, *Aging* (2022). DOI:

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