Newly identified biomarkers may detect early cognitive decline via blood test

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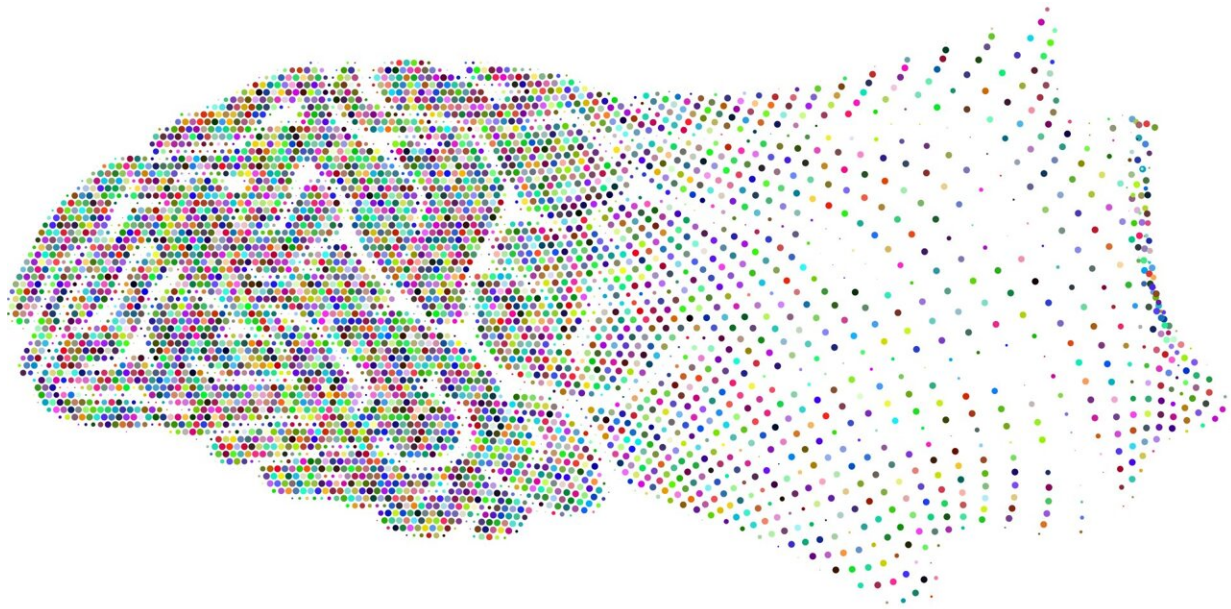

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For some people, extreme stressors like psychiatric disorders or childhood neglect and abuse can lead to a range of health problems later in life, including depression, anxiety and cardiovascular disease. A new study led by researchers in the Penn State Center for Healthy Aging identified genetic indicators that can predict another health problem, the decline of cognitive abilities, among people who have been affected by these extreme stressors.

The team recently published their findings in *Neurobiology of Stress*.

Not everyone who experiences maltreatment as a child or has a psychiatric disorder experiences health problems in later life, but many do, the researchers said. For people whose health is impacted by these extreme stressors, cells age faster, and the body physically begins to break down at an earlier age. This process is known as "accelerated biological aging."

When people age naturally, several cognitive functions decline, including memory, reasoning, executive function and processing speed. Genetic research from investigators around the world has shown mixed results on whether accelerated biological aging starts the cognitive decline process at a younger age.

One study led by researchers from Max Planck Institute of Psychiatry, including Natan Yusupov, co-author on the *Neurobiology of Stress* paper, demonstrated a connection. Other papers, including one led by researchers at Emory University and also published earlier this year, determined that no connection exists.

In the *Neurobiology of Stress* paper, the researchers evaluated two separate population samples and found that accelerated biological aging may serve as a biomarker for cognitive decline.

"Understanding the connection between accelerated biological aging and cognitive decline may help researchers create treatments that help people who have experienced extreme stressors to experience better health," said John Felt, assistant research professor in the Center for Healthy Aging and lead author of the study.

Scientists are looking for genetic markers that can assist in early identification of a variety of health problems that result from extreme

stressors, according to Felt. He said that identification is needed to treat or prevent health problems.

"When addressing a problem like cognitive decline, there are three stages that researchers want to work through: identification, treatment and—if possible—prevention of the problem," Felt said. "We are in the identification phase of understanding how stressors like child maltreatment and psychiatric disorders become embedded in our lives on a cellular level."

Prior work by other researchers indicates that early cognitive decline is detectable for decades before it affects quality of life, Felt said. This creates a period of time when early identification and treatment could be possible.

In this study, the researchers used blood samples and other medical data collected for other studies to examine the relationship between potential genetic indicators of cognitive performance, cognitive performance testing data and incidence of psychiatric disorders or childhood maltreatment.

The data was from two different studies: the Female Growth and Development Study (FGDS) conducted at Penn State and the Biological Classification of Mental Disorders (BeCOME) conducted at the Max Planck Institute of Psychiatry in Germany. FGDS contained data on 86 women in the United States between the ages of 29 and 45. BeCOME contained data on 313 women and men in Germany between the ages of 18 and 66.

The researchers modeled the data and demonstrated that accelerated biological aging can predict lower cognitive ability and slower processing speed. However, the specific genetic indicators that demonstrate this relationship differed between the FGDS cohort data and the BeCOME

cohort data.

Felt said the researchers believe that different genetic indicators predict cognitive decline in the two datasets because the studies were designed differently. The BeCOME cohort covered an age range of 48 years, while the FGDS cohort covered an age range of only 16 years. The restricted age range in the FGDS cohort may have made it insensitive to the indicator that worked on the BeCOME sample, while the FGDS sample indicator may be too limited to apply to the broader BeCOME group. Felt cautioned that other differences—like the racial composition of the two cohorts—could also account for these results.

"My previous research collaborations in this area have focused on accelerated biological aging among people who experienced childhood sexual abuse, but this finding extends to people who have psychiatric conditions," Felt said.

"Cognitive decline can undermine your personal and professional life, especially for people who also have a psychiatric condition. Our research could lead to blood tests for early identification of cognitive decline and eventually to personalized treatments that support cognitive function in people with accelerated biological aging."

More information: John M. Felt et al, Epigenetic age acceleration as a biomarker for impaired cognitive abilities in adulthood following early life adversity and psychiatric disorders, *Neurobiology of Stress* (2023). DOI: 10.1016/j.ynstr.2023.100577

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