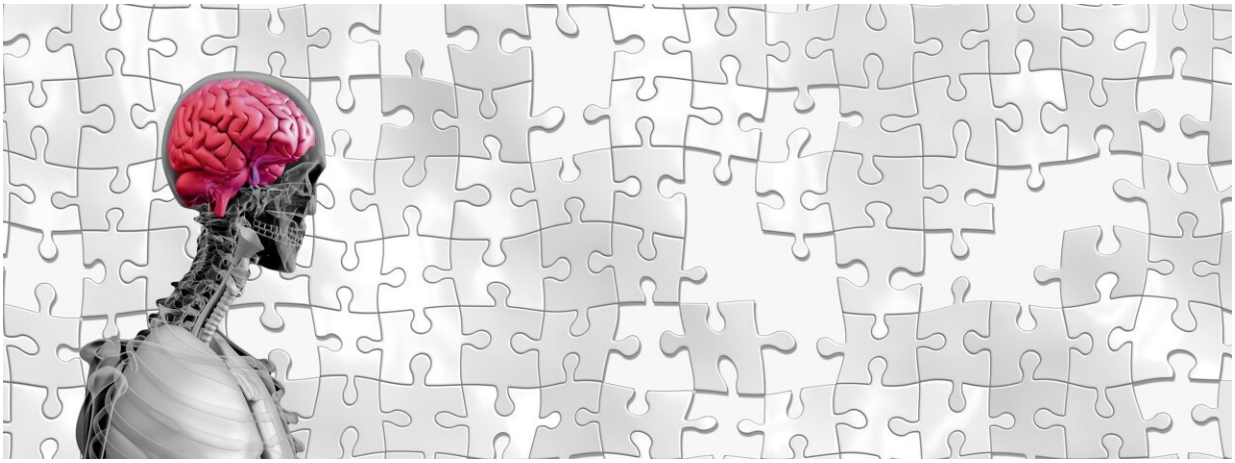
New test could detect Alzheimer's disease 3.5 years before clinical diagnosis

January 26 2023



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New research from the Institute of Psychiatry, Psychology & Neuroscience (IoPPN) at King's College London has established a blood-based test that could be used to predict the risk of Alzheimer's disease up to 3.5 years before clinical diagnosis.

The study, published in the journal *Brain*, supports the idea that components in the human blood can modulate the formation of new brain cells, a process termed neurogenesis. Neurogenesis occurs in an important part of the brain called the hippocampus that is involved in learning and memory.

While Alzheimer's disease affects the formation of new brain cells in the hippocampus during the early stages of the disease, previous studies have only been able to study neurogenesis in its later stages through autopsies.

To understand the early changes, researchers collected blood samples over several years from 56 individuals with Mild Cognitive Impairment (MCI), a condition where someone will begin to experience a worsening of their memory or cognitive ability. While not everyone experiencing MCI goes on to develop Alzheimer's disease, those with the condition progress to a diagnosis at a much higher rate than the wider population. Of the 56 participants in the study, 36 went on to receive a diagnosis of Alzheimer's disease.

Dr. Aleksandra Maruszak, one of the study's joint first authors from King's IoPPN explains, "In our study, we treated brain cells with blood taken from people with MCI, exploring how those cells changed in response to blood as Alzheimer's disease progressed."

In studying how blood affected the brain cells, the researchers made several key discoveries. The blood samples collected from participants over the years who subsequently deteriorated and developed Alzheimer's disease promoted a decrease in cell growth and division and an increase in apoptotic cell death (the process by which cells are programmed to die). However, the researchers noted that these samples also increased the conversion of immature brain cells to hippocampal neurons.

While the underlying reasons for the increased neurogenesis remain unclear, the researchers theorize that it may be an early compensating mechanism for the neurodegeneration (loss of brain cells) experienced by those developing Alzheimer's disease.

Professor Sandrine Thuret, the study's lead author from King's IoPPN said, "Previous studies have shown that blood from young mice can have

a rejuvenating effect on the cognition of older mice by improving hippocampal neurogenesis. This gave us the idea of modeling the process of neurogenesis in a dish using human brain cells and human blood. In our study, we aimed to use this model to understand the process of neurogenesis and to use changes in this process to predict Alzheimer's disease and found the first evidence in humans that the body's circulatory system can have an effect on the brain's ability to form new cells."

When the researchers used only the blood samples collected furthest away from when the participants were diagnosed with Alzheimer's disease, they found that the changes in neurogenesis occurred 3.5 years prior to a clinical diagnosis.

Dr. Edina Silajdžić, the study's joint first author added, "Our findings are extremely important, potentially allowing us to predict onset of Alzheimer's early in a non-invasive fashion. This could complement other blood-based biomarkers that reflect the classical signs of the disease, such as the accumulation of amyloid and tau (the 'flagship' proteins of Alzheimer's disease)."

Dr. Hyunah Lee, the study's joint first author said, "It is now essential to validate these findings in a bigger and more diverse group of people. We are excited about the potential applications of the blood-based test we used. For example, it can help stratify individuals with memory problems for a clinical trial of disease-modifying drugs for Alzheimer's."

The researchers say that these findings could present an opportunity to further understand the changes the brain goes through at the earliest stages of Alzheimer's disease.

More information: Aleksandra Maruszak et al, Predicting progression to Alzheimer's disease with human hippocampal progenitors exposed to

serum, *Brain* (2023). DOI: 10.1093/brain/awac472