

Cerebral blood flow decreases in asymptomatic stages of Alzheimer's

- This is one of the main conclusions of a study published in *Alzheimer's and Dementia* and led by the Barcelona*beta* Brain Research Center, Pasqual Maragall Foundation's research center.
- Lower blood flow, measured with a new, especially sensitive MRI technique, is associated with the accumulation of amyloid-beta protein in the brain.
- The work is the result of an international collaboration spanning experts in Alzheimer's research, MRI sequences and clinical settings.
- The analysis includes data from participants from the Alfa cohort, promoted by "la Caixa" Foundation.

Barcelona, July 22, 2024 – A multilateral collaboration led by the [Barcelona*beta* Brain Research Center](#) (BBRC), the research center of the Pasqual Maragall Foundation, **has been able to measure, thanks to a new Magnetic Resonance Imaging (MRI) sequence, a decrease in the cerebral blood flow in the very first stages of Alzheimer's disease**, before the clinical symptoms appear. The project has involved experts in the development of novel MRI sequences, clinical professionals at the Hospital del Mar and collaborators providing state-of-the-art biomarkers of Alzheimer's disease.

The team has used a new technique, *Time-encoded Arterial Spin Labeling (teASL)*, to detect **the very early changes in the cerebral blood flow of the study participants**. The results of the study, published in the scientific journal *Alzheimer's & Dementia*, show that people affected by the pathology of the disease also display lower blood flow in specific areas of the brain during its first stages.

Measuring the reduction

One of the first processes that are activated in the brain due to the presence of Alzheimer's pathology (that is, an accumulation of amyloid beta and tau proteins), is a decrease in the cerebral blood flow. Blood supplies oxygen and glucose to the brain and, therefore, needs to be maintained within normal levels to ensure the brain's health and proper functioning. **Alterations in cerebral blood flow can precede or accompany various neurological conditions**, including Alzheimer's disease and, as such, accurately measuring it is vital for understanding these conditions. Arterial Spin Labeling (ASL) techniques allow to measure the cerebral blood flow using MR pulse sequences.

"Until now, the ASL techniques available allowed us to measure and compare cerebral blood flow in people with single delay time. This refers to the time it takes for the arterial blood to transit from the carotid arteries (where it is tagged) to the brain region of interest (known as arterial transit time)", explains **Dr. Michalis Kassinopoulos, postdoctoral researcher at the BBRC and one of the main authors of the study.** *"However, these methods were not optimal to detect*

subtle changes in the very early stages of the disease, as they were influenced by different factors that affect blood transit time variations across individuals as well as across brain regions within an individual", he adds.

Thanks to a research collaboration with Philips, the BBRC has had access to a new ASL MRI sequence developed by Leiden University Medical Center, known as *time-encoded ASL (teASL)*. **This is a more sensitive and accurate tool reducing the intra-subject arterial transit time differences in the estimation of the cerebral blood flow.** Researchers have used teASL to measure cerebral blood flow and investigate its association with amyloid and tau pathology, both of which are implicated in Alzheimer's disease. Additionally, they have examined the relationship of decreases in cerebral blood flow with biomarkers in cerebrospinal fluid related to synaptic dysfunction and neurodegeneration, as well as cognitive performance. This way, the study has demonstrated, for the first time in asymptomatic individuals, that the levels of cerebral blood flow are associated with markers of tau pathophysiology, synaptic dysfunction and neurodegeneration.

Findings to define future prevention strategies

For this study, a total of 59 participants were separated into three groups: 24 healthy participants without cognitive impairment or amyloid protein accumulation in the brain (the "control" group); 18 healthy volunteers without cognitive impairment but with amyloid pathology present, and 17 patients from the Medical Research Unit at the Hospital del Mar in Barcelona, affected by the disease. Out of the healthy participants, around 30 belong to the Alfa study, promoted by "la Caixa" Foundation.

The study provides evidence that a reduced cerebral blood flow is not only present in persons in symptomatic Alzheimer's stages, but also in cognitively unimpaired individuals harboring cerebral amyloid-beta pathology. *"Reduced cerebral blood flow is an earlier event in the pathological cascade than previously thought, spanning preclinical stages", asserts Dr. Juan Domingo Gispert, collaborator of the BBRC and corresponding author of the study. "These findings provide insight into the role of this early process in the disease, and can help shape future prevention strategies", he concludes.*

Bibliographic reference

Falcon C, Montesinos P, Václavů L, Kassinosopoulos M, et al. Time-encoded ASL reveals lower cerebral blood flow in the early AD continuum. *Alzheimer's Dement.* 2024; 1-15. <https://doi.org/10.1002/alz.14059>

About Alzheimer's disease

It is estimated that Alzheimer's disease and Alzheimer's dementia currently affect 900,000 people in Spain, which translates into one in ten people over 65 years old and a third of those over 85. These age-related pathologies are one of the leading causes of mortality, disability and dependency. If effective care is not found and with life expectancy increasing, in the year 2050 the number of cases could triple in the world, exceeding a million and a half people in Spain, which could collapse the health and care systems.

About the Barcelonaβeta Brain Research Center and the Pasqual Maragall Foundation

The Barcelonaβeta Brain Research Center (BBRC) is the research center of the Pasqual Maragall Foundation, promoted by the "la Caixa" Foundation since its creation, dedicated to the prevention of Alzheimer's disease and the study of the cognitive functions affected in the healthy and pathological aging.

The Pasqual Maragall Foundation is a non-profit organization that was created in April 2008, in response to the commitment made by Pasqual Maragall, former mayor of Barcelona and former president of the Generalitat of Catalonia, when he publicly announced that he had been diagnosed with Alzheimer's disease. The Foundation's mission is to promote research to prevent Alzheimer's and offer solutions that improve the quality of life of affected people and their caregivers.

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