Amyloid beta accumulation confirmed to cause early brain damage in Alzheimer's

- **A groundbreaking study led by Dr. Raffaele Cacciaglia from the BarcelonaBeta Brain Research Center (BBRC) has shown that amyloid accumulation on its own can cause brain atrophy and cognitive decline, even without elevated levels of the tau protein.**

- **The finding opens the door to preventive approaches and earlier treatments, which could slow the progression of the disease.**

- **This breakthrough has been made possible thanks to 360 middle-aged volunteers without cognitive impairment from the Alfa cohort, promoted by "la Caixa" Foundation.**

Barcelona, February 3rd, 2025 – A study by the BarcelonaBeta Brain Research Center (BBRC), a research center of the Pasqual Maragall Foundation, has identified that **the accumulation of beta amyloid can, on its own, cause brain damage in the early stages of Alzheimer's**, even without elevated levels of the tau protein. This finding, published in the journal *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, provides new clues about how this disease, which affects more than 900,000 people in Spain, develops.

Until now, it was believed that neurodegeneration in Alzheimer's, especially that affecting **the medial temporal lobe of the brain, a region essential for memory function**, occurred only when two key proteins were present: beta amyloid and tau. However, **this new work suggests that the accumulation of beta amyloid can, on its own, trigger brain damage** and memory loss in the early stages, even without the presence of high levels of tau.

To reach this conclusion, the BBRC research team, led by **Dr. Raffaele Cacciaglia**, has worked with two independent cohorts of people without cognitive impairment, volunteers of the Alfa cohort promoted by "la Caixa" Foundation, to analyze data through high-resolution magnetic resonance imaging and markers of the disease. **The results show that the accumulation of beta amyloid can predict structural changes in the brain and possible memory impairment before the appearance of obvious symptoms.**

"In recent years, the first drugs have been approved to reduce the accumulation of beta amyloid in the brain of people in the early stages of Alzheimer's. This advance suggests that intervening at early stages, before symptoms appear, could slow the progression of the disease. Beta amyloid appears to directly affect the hippocampus, a key region for memory, so acting early could significantly reduce the risks associated with Alzheimer's," says **Dr. Raffaele Cacciaglia, BBRC researcher and leader of the study.**

A step closer to preventing Alzheimer's

The study has analyzed samples of cerebrospinal fluid from the 360 volunteers from the Alfa cohort promoted by "la Caixa" Foundation and has used cutting-edge technologies to capture detailed images of the hippocampus and other brain structures using advanced magnetic resonance techniques. Furthermore,

data from Alfa participants have been matched to the EPAD validation cohort, which has no symptoms of Alzheimer's disease or presence of tau protein.

The discovery that amyloid beta on its own can cause initial atrophy in critical brain regions underscores the importance of early detection and prevention. It also reinforces the need for clinical trials targeting people with risk profiles, before Alzheimer's disease begins to manifest.

Bibliographic reference

Cacciaglia R, Falcón C, Benavides GS, et al.; for the ALFA study (2025). Soluble A*β* pathology predicts neurodegeneration and cognitive decline independently on p-tau in the earliest Alzheimer's *continuum*: evidence across two independent cohorts. *Alzheimer's Dement*; e14415. https://doi.org/10.1002/alz.14415

Alzheimer's disease in numbers

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 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.

The Pasqual Maragall Foundation has the support of:

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