

Early action to control cardiovascular risk factors preserves brain metabolism

- A study published in *The Lancet Healthy Longevity* shows that brain metabolism, detected with advanced imaging techniques, declines more sharply in middle-aged people with a sustained high cardiovascular risk over 5 years
- Atherosclerosis and its associated risk factors, in addition to being the main causes of cardiovascular disease, are also implicated at a lower degree in the cerebral alterations typical of Alzheimer's disease
- The CNIC study could have major implications for clinical practice as it supports the implementation of primary cardiovascular prevention strategies early in life as a valuable way to achieve healthy cerebral longevity

Madrid, August 31, 2023. Cardiovascular disease and dementia frequently occur together in elderly people. Nevertheless, few longitudinal studies have examined how atherosclerosis and its associated risk factors affect brain health from middle age. Now, a new study by scientists at the Centro Nacional de Investigaciones Cardiovasculares (CNIC), in Madrid, with the participation of the research center of the Pasqual Maragall Foundation, the BarcelonaBeta Brain Research Center (BBRC), provides new data on this relationship; the results confirm the importance of controlling traditional cardiovascular risk factors, such as hypertension, cholesterol, diabetes, smoking, and a sedentary lifestyle, and not only to preserve cardiovascular health, but also to prevent Alzheimer's disease and other dementias.

Published in *The Lancet Healthy Longevity*, the CNIC study shows that atherosclerosis—the accumulation of fatty deposits in the arteries—and its associated risk factors, in addition to being the main cause of cardiovascular disease, are also implicated in the cerebral alterations typically found in Alzheimer's disease, the most frequent cause of dementia.

According to **CNIC General Director Dr. Valentín Fuster**, an author on the study, the new findings are important because they open up the possibility of treating a modifiable disorder (cardiovascular disease) to prevent the development of a disease for which there is currently no curative treatment (dementia). *"The sooner we act to control cardiovascular risk factors, the better it is for our brain health,"* said Dr. Fuster.

"Everybody knows that a healthy lifestyle and controlling cardiovascular risk factors are important for preventing a heart attack," continued Dr. Fuster. *"Nevertheless, the additional information linking the same risk factors to a decline in brain health could further increase awareness of the need to acquire healthy habits from the earliest life stages."*

In 2021, CNIC scientists discovered that the presence of cardiovascular risk factors and subclinical (presymptomatic) atherosclerosis in the carotid arteries (the arteries that supply the brain) was associated with lower glucose metabolism in the brains of apparently healthy 50-year-old participants in the PESA-CNIC-Santander study (Cortés-Canteli & Gispert et al. JACC. 2021). Glucose metabolism in the brain is considered an indicator of brain health.

The PESA-CNIC-Santander study, directed by Dr. Fuster, is a prospective study that includes more than 4000 asymptomatic middle-aged participants who have been exhaustively assessed for the presence and progression of subclinical atherosclerosis since 2010.

Dr. Fuster's team, led by Drs. Marta Cortés Canteli and Juan Domingo Gispert, have continued to monitor the cerebral health of these participants over 5 years. Their research shows that individuals who maintained a high cardiovascular risk throughout this period had a more pronounced reduction in cerebral glucose metabolism, detected using imaging techniques such as positron emission tomography (PET).

"In participants with a sustained high cardiovascular risk, the decline in cerebral metabolism was three times greater than in participants who maintained a low cardiovascular risk," commented **Catarina Tristão-Pereira, first author on the study and INPhINIT fellow.**

Glucose is the main energy source for neurons and other brain cells. *"If there is a sustained decline in cerebral glucose consumption over several years, this may limit the brain ability to withstand neurodegenerative or cerebrovascular diseases in the future,"* explained **Dr. Gispert, an expert in neuroimaging at the CNIC and Barcelonaβeta Research Center.**

Through a collaboration with Drs Henrik Zetterberg and Kaj Blennow, world experts in the identification of new blood biomarkers at the University of Gothenburg in Sweden, the CNIC team discovered that the individuals showing this metabolic decline already show signs of neuronal injury. *"This is a particularly important finding because neuronal death is irreversible",* said **Dr. Cortés Canteli, a neuroscientist at the CNIC and a Miguel Servet fellow at the Fundación Jiménez Díaz Health Research Institute.**

The CNIC team also discovered that the progression of subclinical atherosclerosis in the carotid arteries over 5 years is linked to a metabolic decline in brain regions vulnerable to Alzheimer's disease, in addition to the effect of cardiovascular risk factors. *"These results provide yet another demonstration that the detection of subclinical atherosclerosis with imaging techniques provides highly relevant information,"* said **Dr. Fuster, who is the principal investigator on the PESA study.** *"The interaction between the brain and the heart is a fascinating topic, and with this study we have seen that this relationship begins much earlier than was thought."*

The scientists conclude that in light of these results, *"carotid screening has great potential to identify individuals at risk of cerebral alterations and cognitive decline in the future."* In the published article they write, *"this work could have important implications for clinical practice since it supports the implementation of primary cardiovascular prevention strategies early in life as a valuable approach*

for a healthy cerebral longevity.”

*“Although we still don’t know what impact this decline in cerebral metabolism has on cognitive function, the detection of neuronal injury in these individuals shows that the earlier we start to control cardiovascular risk factors, the better it will be for our brain,” concluded **Dr. Cortés Canteli**.*

The PESA study is equally financed by the CNIC and Banco Santander. The PESA study also receives funding from the Instituto de Salud Carlos III (ISCIII, PI15/02019 & PI20/00819), the European Regional Development Fund (ERDF - A Way to Build Europe) and the European Social Fund (ESF - Investing in Your Future). The present study received funding from the BrightFocus Foundation and a Leonardo Investigadores y Creadores Culturales award from the BBVA Foundation. The CNIC is supported by the ISCIII, the Ministerio de Ciencia e Investigación (MCIN), and the Pro-CNIC Fundacion. The study included the participation of investigators in three Spanish research networks (CIBER): Cardiovascular Disease (CiberCV); Frailty and Healthy Aging (CiberFES); and Bioengineering, Biomaterials, and Nanomedicine (Ciber-BBN).

About the CNIC

The Centro Nacional de Investigaciones Cardiovasculares (CNIC), directed by Dr. Valentín Fuster, is dedicated to cardiovascular research and the translation of knowledge gained into real benefits for patients. The CNIC, recognized by the Spanish government as a Severo Ochoa center of excellence, is financed through a pioneering public-private partnership between the government (through the Carlos III Institute of Health) and the Pro-CNIC Foundation, which brings together 12 of the most important Spanish private companies.

About the BarcelonaBeta Brain Research Center and the Pasqual Maragall Foundation

The BarcelonaBeta 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.

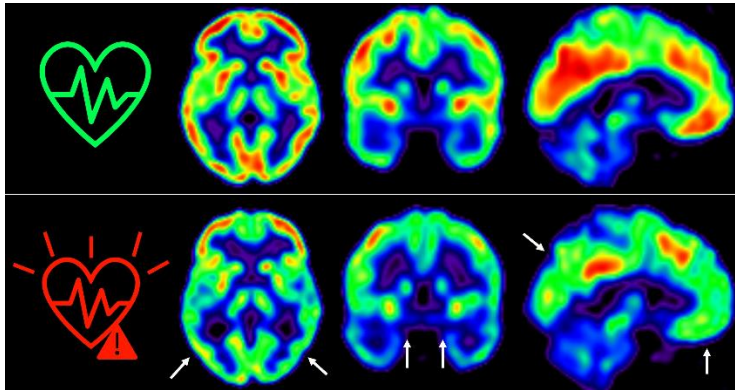


Image: The image represent glucose uptake in the brain measured by positron emission tomography in middle-aged individuals with low (top) or high (bottom) sustained cardiovascular risk over 5 years. The colors represent cerebral glucose consumption, with red indicating higher consumption and blue lower consumption.

Information and interview requests:

Fátima Lois: CNIC Head of Communications. flois@cnic.es / Tel 639282477

Rafael Ibarra: CNIC Communications Office. ribarra@cnic.es / 914531200. Ext 4232

Paula Talero: Communication BBRC / FPM. ptalero@fpmaragall.org / 683 28 60 06