The Lancet Healthy Longevity: Early action to control cardiovascular risk factors preserves brain metabolism

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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*

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 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, 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.

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