Combining diet, physical exercise, cognitive training, and a green tea compound reduces the risk of dementia

- **This is indicated by the results of the PENSA study, a clinical trial conducted jointly by the Research Institute of Hospital del Mar and the Barcelonaβeta Brain Research Center, the research center of the Pasqual Maragall Foundation. The study concludes that combining a healthy lifestyle program with epigallocatechin gallate (EGCG), a natural compound found in green tea, could offer sustained cognitive benefits in people at high risk of developing Alzheimer's disease.**

- **Over the course of one year, around one hundred cognitively healthy volunteers, but in stages potentially prior to the onset of dementia, were monitored. They were divided into three groups. One group received only healthy lifestyle advice. The other two groups underwent a lifestyle improvement intervention program combined with either EGCG or placebo.**

- **Almost half of the participants who received the lifestyle program combined with EGCG improved their cognition, compared to 30% of those in the lifestyle program combined with the placebo group. These cognitive benefits in the EGCG group were maintained after the treatment ended.**

- **The study also highlights the effect of following a healthy lifestyle. Compared to participants who only received healthy lifestyle advice, those who completed the full intervention program improved their cognition up to 4.5 times more if they took EGCG, and up to 3 times more if they took placebo. Furthermore, both intervention groups reduced the risk of developing dementia by approximately 25%.**

Barcelona, July 31, 2025 - Researchers from the Research Institute of Hospital del Mar and the Barcelonaβeta Brain Research Center, the research center of the Pasqual Maragall Foundation, **have demonstrated the benefits of following healthy lifestyle habits in preventing cognitive decline and the risk of dementia**. Moreover, if a green tea compound, **epigallocatechin gallate** (EGCG), is added, the effects increase and are sustained over time. According to the results of the PENSA study (Prevention of cognitive decline in APOE-ε4 carriers with Subjective Cognitive Decline after EGCG and a multimodal intervention), published in The Journal of Prevention of Alzheimer's Disease, participants who completed **the full intervention program improved their cognition up to 4.5 times more**, and their risk of developing dementia was reduced by approximately 25%.

The work consisted of a randomized, placebo-controlled clinical trial (with respect to EGCG), involving 129 cognitively healthy individuals aged 60 to 80, **at high risk of Alzheimer's disease** due to meeting criteria for **subjective cognitive decline** (SCD) and being carriers of the genetic risk factor APOE-ε4, which increases the risk of Alzheimer's disease up to fivefold. People with subjective cognitive decline perceive a decrease in cognitive abilities such as memory or attention, although this decline is not detectable with standard neuropsychological tests. It is considered a possible precursor to mild cognitive impairment (MCI) and may be associated with a higher risk of developing Alzheimer's disease. The PENSA study is the only one conducted worldwide in this high-risk population.

Positive and Long-lasting Effect

Participants were divided into three groups. In the first, volunteers underwent a multimodal lifestyle intervention including healthy eating guidelines based on the Mediterranean diet, physical exercise, and cognitive stimulation, with visits to a nutritionist, guided gym classes, psychoeducation, access to a cognitive training platform, promotion of social interaction, and monitoring of physical activity and sleep quality using an activity wristband. At the same time, they received epigallocatechin gallate (EGCG). The EGCG dose was adjusted to each participant's body weight and remained within the safety limits established by health authorities. The second group received the same intervention but took a placebo instead of EGCG. The third, control group received only healthy lifestyle recommendations at the beginning of the study. The study lasted 12 months, plus an additional three months of follow-up without intervention.

The results demonstrate the positive effects of multimodal intervention. *"In the groups treated with this type of intervention, not only does cognition improve significantly, but there is also a reduction in dementia risk compared to the control group. The magnitude of the changes is very relevant and is the largest observed so far in similar prevention studies. The study also demonstrates the absence of adverse effects related to EGCG treatment*", explains **Dr. Rafael de la Torre**, who led the PENSA study and coordinates the Integrated Pharmacology and Systems Neuroscience Research Group at the Research Institute of Hospital del Mar. While the dementia risk, measured by the LIBRA index (Lifestyle for Brain Health Risk Score) and calculated based on various factors (chronic health problems, biochemical markers, age, gender, and years of formal education), did not change in the control group during the twelve months, the groups undergoing intervention **reduced this risk by between 23% and 27%**.

Among the two groups receiving the lifestyle intervention, cognition improved **50% more** in the EGCG group compared to placebo. This global cognition improvement at the end of the study also reflects the fact that **48% of participants who received both lifestyle intervention and EGCG improved their cognition**, compared to 27% of participants who received the lifestyle intervention with placebo. It is important to note that without any intervention, people with subjective cognitive decline and APOE-ε4 carriers are expected to experience **spontaneous cognitive decline over time**.

Both **lifestyle intervention** groups showed **improvements in global cognition** and **executive functions**, a set of skills that allow focusing attention, remembering instructions, planning, organizing, decision-making, and managing multiple tasks simultaneously. *"These results are relevant because executive functions, together with memory, are among the cognitive domains most early affected in Alzheimer's disease, and their integrity is key to maintaining independence in daily activities",* explains **Dr. Gonzalo Sánchez**, PENSA and BBRC researcher.

Sustained Cognitive Improvement Over Time

Finally, participants were reassessed three months after the end of the trial, once the intervention had concluded. It was observed that cognitive effects were more sustained in those who participated in the intervention and took EGCG. Specifically, the EGCG group showed greater improvements in memory and

semantic fluency compared to the lifestyle intervention with the placebo group. *"This study is one of the first worldwide to show that combining these multimodal interventions with cognition-enhancing compounds has additive effects; that is, using these substances helps maintain the positive effects of lifestyle changes",* points out **Dr. Laura Forcano**, PENSA and Hospital del Mar Research Institute researcher.

The research is framed within the FINGER 2.0 model, which combines lifestyle interventions with bioactive compounds to maximize cognitive benefits. The original FINGER study, conducted in Finland, demonstrated that multimodal lifestyle interventions can improve cognition in people at high risk of dementia. EGCG is a flavonoid found in green tea that acts through multiple neuroprotective mechanisms. Previous studies have shown it has antioxidant and anti-inflammatory properties, improves synaptic plasticity, regulates glucose metabolism, and may reduce the accumulation of toxic proteins associated with Alzheimer's disease.

"Part of the success of the PENSA study is due to the high adherence to treatment and healthy lifestyle guidelines demonstrated by participants, substantially improving their diet, cardiovascular health, activity, physical functionality, and quality of life", notes **Dr. Natàlia Soldevila,** also a researcher at Hospital del Mar and the BarcelonaBeta Brain Research Center. *"This study represents an important advance in precision prevention of Alzheimer's disease",* adds **Dr. Oriol Grau**, researcher at the BarcelonaBeta Brain Research Center. "*By focusing on APOE-ε4 carriers with subjective cognitive decline, we are targeting the intervention to those most likely to benefit from it, following the concept of personalized medicine*".

The researchers point out that these results are proof of concept and that more research is needed to confirm these findings in larger and more diverse populations with longer follow-up periods. It will also be important to explore the underlying mechanisms driving cognitive changes and to determine the optimal intensity and dosage of the intervention.

In the project design and the proposal of activities for the different interventions, patients and family members participated for the first time, some of whom are members of the Hospital del Mar Patient Forum. The project received support from Grand Fontaine Laboratories, providers of the green tea preparation (Font-Up); the food company Caprabo, with a discount card on basic Mediterranean diet products; the Claror Sports Foundation, where the structured physical activity took place in the gym; the tech companies Fitbit, providing the activity wristband, and NeuronUp, provider of the telematic cognitive training platform. Support was also received from the Casal Municipal de la Gent Gran Mediterrània and the Barceloneta Civic Center.

The PENSA study was conducted between November 2019 and March 2023, including a 15-month follow-up period. The project received a $1 million grant from the Alzheimer's Association in the United States and is part of the global primary dementia prevention project World Wide FINGERS. It also received €150,000 in funding from the Carlos III Health Institute (ISCIII).

Reference article:

Forcano L, Soldevila-Domenech N, Boronat A, Sánchez-Benavides G, Puig-Pijoan A, Lorenzo T, Aldea-Perona A, Suárez-Calvet M, Cuenca-Royo A, Gispert JD, Gomis-Gonzalez M, Minguillón C, Diaz-Pellicer P, Fauria K, Piera I, Langohr K, Dierssen M, Pizarro N, Mur-Gimeno E, Grau-Rivera O, Molinuevo JL, de la Torre R; PENSA working group. A multimodal lifestyle intervention complemented with epigallocatechin gallate to prevent cognitive decline in APOE- ε4 carriers with Subjective Cognitive Decline: a randomized, double-blinded clinical trial (PENSA study). J Prev Alzheimers Dis. 2025 Jul 14:100271. doi: 10.1016/j.tjpad.2025.100271.

Alzheimer's disease in numbers

It is currently estimated that Alzheimer's disease and neurodegenerative diseases affect 900,000 people, a figure that translates to one in ten of those over 65 years of age and a third of those over 85. These diseases are one of the main causes of mortality, disability, and dependency. If an effective cure is not found and life expectancy continues to increase, the number of cases worldwide could triple by 2050, exceeding one and a half million people in Spain alone, a situation that could lead to the collapse of healthcare and care systems.

About Hospital del Mar Research Institute

The Hospital del Mar Research Institute in Barcelona is a scientific research center in the field of biomedicine and health sciences, organized into five major research programs: Cancer, Epidemiology and Public Health, Biomedical Informatics, Neurosciences and Translational Clinical Research. Formed by about 700 professionals, it is among the ten Spanish institutions with the greatest scientific impact in the health area.

It is a CERCA center of the Generalitat de Catalunya and is accredited as a Health Research Institute by the Carlos III Health Institute.

About the BarcelonaBeta Brain Research Center and the Pasqual Maragall Foundation

The BarcelonaBeta Brain Research Center (BBRC) is the research centre of the Pasqual Maragall Foundation, supported by the "la Caixa" Foundation since its creation, dedicated to the prevention of Alzheimer's disease and the study of cognitive functions affected in healthy and pathological aging. BBRC research focuses on the preclinical phase of Alzheimer's disease, the period before the first symptoms appear, when changes in the brain associated with the disease already occur. The BBRC has more than 100 professionals dedicated to contributing to the forefront of research into Alzheimer's disease and other neurodegenerative diseases.

The Pasqual Maragall Foundation is a non-profit organization founded in April 2008 in response to the commitment made by Pasqual Maragall, former mayor of Barcelona and former president of the Generalitat de Catalunya, 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 disease and offer solutions that improve the quality of life of those affected and their families.

The Pasqual Maragall Foundation has the support of more than 93,000 members and of:

Press contacts:

Comunication Agency
ATREVIA
Esther Seró/ Cristina Campabadal
fpmaragall@atrevia.com
667 632 909 / 644 24 11 67

Communication department of the Hospital del Mar Research Institute/Hospital del Mar

Marta Calsina
mcalsina@researchmar.net
93 316 06 80

David Collantes
dcollantes@hmar.cat
600 40 27 85