

Press Release

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International study led by the UKE

Alzheimer's: Identification of genetic variants associated with the speed of cognitive function loss

Memory loss is the most important symptom of early-stage Alzheimer's dementia and occurs before other cognitive functions deteriorate. In an international study conducted with scientists of the University of Antioquia (Colombia), researchers at the Medical Center Hamburg-Eppendorf have identified genetic variants that are associated with the speed at which these cognitive abilities decline. Genetic variants in olfactory receptors play a particular role in this context. The researchers have published their results in the journal *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*.

This study is based on examinations of patients belonging to a population in Colombia comprised of 5,000 persons. They are afflicted by the so-called Paisa mutation, a particularly severe form of Alzheimer's with an early onset. The researchers compared this hereditary form of Alzheimer's with age-related, so-called sporadic cases of the disease. For the latter form of the disease, they could correlate 227 genetic variants of different functionality to the rate of memory loss; and to the hereditary variant, 172. They found that corresponding genetic variants in olfactory receptors exerted a significant influence. The researchers also found that, in the cerebral cortex, there were neurons without connection to the sense of smell that had characteristics of the primarily affected olfactory receptor. It has been known for some time that the sense of smell and the loss of olfactory sensitivity can be linked to various dementia diseases. Thus, for example, the loss of olfactory sensitivity can be an early symptom of Alzheimer's disease prior to the onset of dementia.

"The findings that genetic variants in olfactory receptors influence the rate at which certain memory traits deteriorate in Alzheimer's disease, and that involved olfactory receptors are also manifest in brain neurons, open up new avenues for understanding cognitive deterioration in this disease," says lead author Dr. Diego Sepulveda-Falla, Institute of Neuropathology at the UKE. "Our study results could thus contribute to therapeutic approaches to slow down memory loss in Alzheimer's dementia," adds Dr. Susanne Krasemann from the Institute of Neuropathology.

The scientists around the UKE researchers and their Colombian colleagues Dr. Mauricio Arcos-Burgos and Dr. Francisco Lopera also found that, in particular, a faster deterioration in memory function is associated with the presence of the corresponding genetic variants. Above all, this

applies to visual-spatial memory, i.e. the ability to remember the exact distribution of objects in two- and three-dimensional space. In cases concerning families, the speed at which this cognitive function deteriorates was more likely to be attributed to the genetic background than in sporadic Alzheimer's disease. In the latter, the rate at which word memory deteriorates is more often associated to genetic causes.

Literature

Sepulveda-Falla, Vélez, Acosta-Baena et al. Genetic Modifiers of Cognitive Decline in PSEN1 E280A Alzheimer's disease. *Alzheimer's & Dementia*, 2024. DOI: doi.org/10.1002/alz.13754.

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The Medical Center Hamburg-Eppendorf (UKE)

Since its foundation in 1889, the Medical Center Hamburg-Eppendorf (UKE) has been one of the leading clinics in Europe. With about 14,900 employees, the UKE is one of the largest employers in the Free and Hanseatic City of Hamburg. The UKE treats about 543,000 patients a year, 89,000 of whom are inpatients and 454,000 are outpatients. The emphasis in UKE's research are the neurosciences, cardio-vascular research, care research, oncology, as well as infections and inflammations. The UKE educates about 3,400 medical specialists, dentists and midwives.

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