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Decoding the ageing brain - Changes in gene activity detected in different cell types

Ageing is a complex biological process that also takes place in the brain. Researchers have discovered that the gene activity changes in different cell types in the brain. A certain type of neuron is particularly affected. In the long term, the findings could provide starting points for slowing down the ageing process and delaying neurodegenerative diseases such as Alzheimer's-type dementia.

As we age, our brain ages too. Every single cell is subject to this process, which is accompanied by changes in gene activity, among other things. Our brain consists of various cell types, each with specific properties, functions and connections, which together perform the brain's complex computations. Researchers from the Max Planck Institute of Psychiatry wanted to know how the gene activity changes in the different cell types of the brain as we age. To this end, they examined tissue samples from 90 brains of people between the ages of 25 and 85, who had donated their brains to science after their death. The researchers focused on cells from the prefrontal cortex, a region of the brain that is crucial for cognitive processes such as thinking, planning and problem-solving.

Single nucleus RNA sequencing enabled the scientists to investigate changes in the gene activity of individual cell types over the course of ageing for the first time. "We were able to show that gene expression changes in all cell types during the course of ageing, but not necessarily in the same genes," summarizes project leader Anna Fröhlich. She found that in all cell types the activity of genes that are important for synaptic transmission, i.e. communication between neurons, changes with ageing. The activity of genes involved in mRNA processing, i.e. the production of protein molecules, also changes during the ageing process.

Comparison with Alzheimer´s disease

As age is the greatest risk factor for neurodegenerative diseases such as Alzheimer's disease, the researchers compared the age-related changes in gene expression with changes observed in Alzheimer's disease. They found extensive overlaps in certain cell types. This could indicate that continuous, non-pathological changes exceed a threshold at some point and thus turn pathological, so to speak. It is particularly interesting that a certain cell type of inhibitory neurons appears to be particularly affected by both ageing and Alzheimer's disease.

The tissue samples examined came from people with and without psychiatric disorder. A comparison of these two groups showed differences in biological ageing: the gene expression age of people with psychiatric illness was accelerated, meaning that they were "biologically" older. This could be because the activity of some genes changes not only with age but also due to the psychiatric disorder, as the scientists were able to show. This could represent a possible explanation as to why people with psychiatric disorders such as schizophrenia might be particularly susceptible to pathological brain ageing processes.

The findings recently published in the journal Nature Neuroscience could help identify new therapeutic approaches at the molecular level that could influence the ageing process and thus potentially delay dementia. However, this requires extensive further research.

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