Study explores the effects of immune responses on the aging brain

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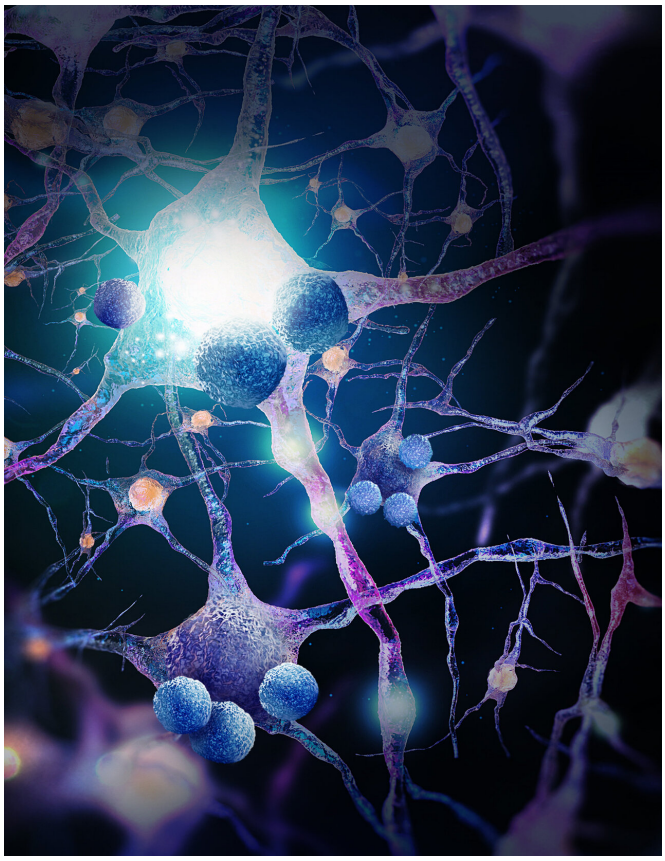

A 3D image illustrating the interactions between natural killer (NK) cells (purple) and neuroblasts (blue) in the aged human brain. Credit: Jin et al.

As human beings age, the functioning of organs gradually deteriorates. While countless past studies have investigated the effects of aging on the human body, brain and on cognition, the neural mechanisms and environmental factors that can accelerate or slow down these effects are not yet fully understood.

The immune system and the nervous system are both known to play a key role in the control of organs in the body. Moreover, past findings suggest that both of these systems change significantly during aging.

Neuroscientific studies have found that as the nervous system ages, the way in which the human body controls immune responses also changes. Nonetheless, how the nervous system's aging process affects immune responses and the consequent impact on the brain's functioning are still poorly understood.

Researchers at Capital Medical University in Beijing and Tianjin Medical University General Hospital have recently carried out a study investigating the possible effects of immune responses on the aging brain. Their paper, published in *Nature Neuroscience*, shows that the deterioration of neuroblasts (i.e., the embryonic cells from which nerve fibers originate) in the aging brain can increase the toxicity of natural killer cells (NK), which leads to impairments in neurogenesis and cognition. NK cells are a class of blood cells that are part of the human immune system.

"Systemic inflammation escalates during the aging process, but the potential impact of immune and inflammatory responses on brain aging remains unknown," Qiang Liu, one of the researchers who carried out the study, told TechXplore. "The goal of our recent study was to understand why immune cells accumulate in the brain during the aging process, and to what extent immune cells influence tissue regeneration and cognition in the aged brain."

Liu and his colleagues carried out their experiments and examinations on brain tissues extracted from aged humans and mice. To investigate the impact of immune responses on neurogenesis and cognition, they used a number of techniques commonly employed by neuroscientists.

"We used single-cell sequencing, lineage tracing and flow cytometry techniques to measure immune cell properties," Liu explained. "Subsequently, we

assessed neurogenesis by immunostaining tissue sections. Finally, we carried out a behavioral assessment to test the impact of immune responses on cognitive function."

Liu and his colleagues observed that NK cells accumulate in a specific area (i.e., the dentate gyrus neurogenic niche) found in both the brains of aged humans and mice. A localized expansion of these cells lets them become increasingly abundant, to the point that they significantly outnumber other types of immune cells.

Neuroblasts in the dentate gyrus region exhibited a set of secretion-related characteristics derived from the interaction of a specific genetic constitution with the environment (i.e., a so-called secretory phenotype), which reinforced the activity of NK cells and their surveillance functions. Ultimately, this led to the NK cells eliminating neuroblasts in the aged brain.

"Essentially, we found that immune cells such as NK cells impair neurogenesis and cognitive function during normal brain aging," Liu said. "Immune modulation targeting immune cells (which accumulate in the aged brain) may thus be useful to improve cognition in the aged population."

The recent study carried out by this team of researchers suggests that the accumulation of NK cells in the aging brain can impair the process through which neurons are formed in the brain, known as neurogenesis. In the future, this important finding could inform the development of more effective treatment strategies for improving cognition in older adults.

"We will now continue to refine our approaches to modulate immune responses in the brain, with an aim to improve cognitive function during brain aging," Liu said.

More information: Neuroblast senescence in the aged brain augments natural killer cell cytotoxicity leading to impaired neurogenesis and cognition. *Nature Neuroscience*(2020). DOI: 10.1038/s41593-020-00745-w