

The Impact Of Aging On Brain Cells' Memory Maintenance Capabilities

Researchers from Nanyang Technological University, Singapore (NTU Singapore), have discovered that communication among memory-coding neurons is disrupted with ageing and can begin in middle age.

The findings, reported in *Nature Communications*, provide new insights into the ageing process of the human mind and could lead to therapies to maintain mental well-being in ageing individuals.

Previous studies used nerve cells from deceased subjects, but the Lee Kong Chian School of Medicine (LKCMedicine) team measured the real-time activity of individual nerve cells in live mice. To make these measurements, they adopted an optical imaging technique that allowed them to understand the function of each neuron by measuring its neural activity in the context of working memory.

The researchers discovered that neurons in the prefrontal cortex showed robust memory coding ability in young mice but this ability diminishes in middle-aged and old mice due to weakening connections among the neurons. These weakened connections cause the mice to take longer to recall and perform tasks.

Lead investigator and Assistant Professor Tsukasa Kamigaki from NTU's LKCMedicine said, "Our study highlights a significant reduction in communication among neurons responsible for encoding memories in the prefrontal cortex – a key factor in age-related working memory decline, which was a neurological process not widely understood until now."

Further experiments showed that the weakening connections begin in middle age, leading to instability of neural circuits in the prefrontal cortex and a poorer ability to hold memory. The team used optogenetic technology to briefly turn off neurons in the brain and found that the working memory circuits in middle-aged mice are particularly sensitive to the interruptions in neural activity.

Co-first author and LKCMedicine Research Assistant Huee Ru Chong said, "Our four-year study shows that the ongoing function of the prefrontal circuits is critical for memory tasks."

Co-first author and LKCMedicine Research Fellow Dr Yadollah Ranjbar-Slamloo said, "We found that the prefrontal cortex in mice stays active when they remember things, like humans."

LKCMedicine Associate Professor Nagaendran Kandiah, Visiting Senior Consultant Neurologist at Singapore's National University Hospital and Khoo Teck Puat Hospital, who is not involved in the study, said, "The exciting findings from the NTU team provide insights into specific neural changes in the prefrontal cortex associated with ageing."

Dr Jun Nishiyama, Assistant Professor in the Neuroscience and Behavioural Disorders programme at Duke-NUS Medical School said, “This groundbreaking study from NTU Singapore offers key neurological insights into age-related working memory decline, highlighting reduced neuronal communication in the mouse prefrontal cortex beginning from middle age.”

The next steps for this project are to investigate more brain-wide neural changes that occur during middle age to understand how proactive interventions may enhance communication among different brain areas.