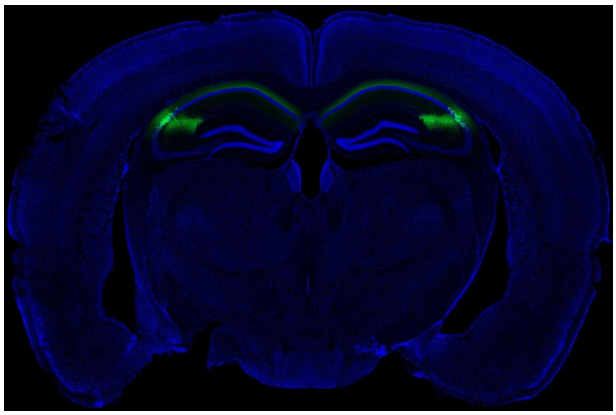
PRESS RELEASE

NUS researchers discover novel mechanisms of memory formation in little-known hippocampal CA2 region

Findings suggest that the release of neuromodulator acetylcholine as a stimulus helps to improve CA2-dependent memory

Hippocampal area CA2 is a critical component of social memory formation, which ultimately guides social interactions. Understanding how neurons in the CA2 region are regulated could hold the key to mechanisms underlying social memory and social behavior.
[Credits: Ananya Dasgupta, former PhD student of NUS Medicine]

Singapore, 22 November 2021 — NUS researchers have discovered that the little-known CA2 hippocampal, a smaller sub-area in the brain, plays a critical role in recording social memories and regulating aspects of social behavior, such as aggression. Social memory is defined as remembering social interactions and recognising familiarities and novelties in these interactions, which shapes our social behaviours.



The CA2 sub-region of the hippocampus, that is essential for social memory is highlighted in green.
[Credits to: Nature]

In the study published in the *Journal of Neuroscience*, Amrita Benoy, a PhD student at the Yong Loo Lin School of Medicine, National University of Singapore (NUS) found that a novel neuronal information processing mechanism, mediated by the modulatory neurotransmitter called acetylcholine, helps shape memory formation in the hippocampal CA2 sub-region. The CA2 sub-region is sandwiched between the CA1 and CA3 sub-regions of the hippocampal. However, due to the small dimensions of the CA2 hippocampal sub-region, this area was previously overlooked in research studies and considered to be a link connecting the CA1 and

CA3 regions of the hippocampal, the main areas which drive the major thrust of memory functions.

The processing of information by the neurons in the CA2 sub-region in the hippocampus as a functional significance only came to light recently due to increased scrutiny and interest. It was found that the CA2 neurons have been releasing different neuromodulators to different regions of the brain, unlike the typical neuromodulators released by the CA1 and CA3 sub-regions. This observation has shed more light into the possibility that neuromodulation by acetylcholine could potentially play a key role in mediating CA2-dependent social memory.

Memories are thought to be formed based on neuronal connections that strengthen and weaken according to the level of stimulation given, known as synaptic plasticity. It has also been observed that despite playing a critical role in memory, the neurons in the CA2 sub-region indicate different mechanisms of memory formation, compared to the neurons in the CA1 and CA3 sub-regions, and lack the neuronal connections that enable storage of memories.

In response to changing external environments and behavioural states, chemical neurotransmitters are released in the brain, which play a pivotal role in regulating the neuronal responses that ultimately shape the learning and behavioural outcomes. The team has gathered that direct stimuli projection, such as the release of acetylcholine from the medial septum and diagonal bands of Broca could mean that the seemingly “plasticity-devoid” state of the neurons in the CA2 sub-region can be corrected to contribute to the stability of memories acquired in social environments to reconcile social memories and behaviours.

This breakthrough in research further affirms what we already understand about how memory formation happens under normal conditions. By understanding the fundamentals of memory formation, it is key to deciphering the causes of behavior disorders, memory loss and memory and behavior impairment such as Alzheimer’s disease. This study will better inform future research that seeks to develop targeted therapies in specific brain regions to treat socio-cognitive deficits in people diagnosed with dementia or Alzheimer’s disease.

Encouraged by this accidental discovery resulting from a graduate thesis research, Associate Professor Sajikumar Sreedharan, Department of Physiology and Healthy Longevity Translational TRP who is supervising Amrita’s research, said, “The research in the CA2 region of the hippocampus is still in its infancy stage; any new research pertaining to this region comes as a significant discovery. We are convinced that our study can enlighten future studies to understand specific brain regions which are associated with cognitive diseases and mental disabilities.”

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Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, 30 university-level research institutes, research centres of excellence and corporate labs focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

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Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through our doors.

In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is Asia's leading medical school and ranks among the best in the world (Times Higher Education World University Rankings 2020 by subject and the Quacquarelli Symonds (QS) World University Rankings by Subject 2020).

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