

PRESS RELEASE

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Researchers from NUS Medicine and the Institute of Mental Health detect early brain changes linked to future psychosis development

Researchers at the Yong Loo Lin School of Medicine, National University of Singapore, and NHG Health's Institute of Mental Health have identified distinct changes in brain network organisation among individuals at clinical high risk for psychosis, providing new insights on how early alterations in brain connectivity may contribute to the development of the disorder.

Singapore, 9 December 2025 — Researchers from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), and NHG Health's Institute of Mental Health (IMH) have mapped how brain networks differ in individuals at Clinical High Risk (CHR) for psychosis, providing a new perspective on the mechanisms underlying the disease onset. Published in [*Molecular Psychiatry*](#), the study utilised advanced neuroimaging methods to identify early, network-level changes in more than 3,000 individuals at varying levels of risk.

The study – led by Dr Siwei Liu, Senior Research Scientist, and Associate Professor Juan Helen Zhou, Director, both at the Centre for Translational Magnetic Resonance Research (TMR), NUS Medicine, and in collaboration with Associate Professor Jimmy Lee, Senior Consultant Psychiatrist and Clinician-Scientist at IMH – sought to determine how brain networks can reveal signs in young individuals with heightened clinical risk of developing psychosis.

Using data from the Enhancing Neuro Imaging Genetics by Meta-Analysis-Clinical High Risk (ENIGMA-CHR) working group, the team analysed brain scans from over 3,000 participants aged between 9.5 and 39.9 years across 31 global sites, including Singapore. The local data came from IMH's Longitudinal Youth-At-Risk Study (LYRIKS), which was initiated in 2008 and led by Assoc Prof Lee, to identify clinical, social, neuropsychological and biological risk factors unique to individuals at high risk of developing psychosis.

The study compared the brain network patterns between young people at high risk for psychosis and healthy individuals, as well as between those who later developed psychosis and those who did not. Using graph theory-based network analysis, they mapped how different brain regions communicate structurally. This approach treats the brain as a complex network, where nodes represent regions and edges represent their connections.

The team observed that in a healthy brain, regions that develop and work together form networks that balance strong local connections with efficient communication across areas. Regional neighbours share both direct and indirect connections, supporting effective local processing. Even with minor damage in one region, neighbouring regions can still communicate through alternate paths. Efficient long-range communication means that even far-apart regions can exchange information quickly using only a few steps.

However, the study found that individuals at high risk for psychosis had less efficiently organised brain networks than healthy individuals. This organisation makes local processing less effective and integrative processing across the brain more difficult. Differences in frontal and temporal brain areas were also linked to whether an individual developed psychosis later in life and how severe their symptoms were, suggesting that brain network patterns may play an important role in the transition to psychosis. The findings also indicated that individuals at high risk for psychosis exhibited early disruptions in the organisation of brain networks, despite showing only mild clinical symptoms.

“Treating the brain as a complex network has allowed us to capture subtle but meaningful differences in communication pathways,” said Dr Liu, first author of the paper. “These findings highlight the potential of brain imaging to detect early alterations and how early changes in network structure may contribute to the onset of psychotic symptoms.” Dr Liu is also a Senior Research Scientist at the Centre for Sleep and Cognition, NUS Medicine.

Assoc Prof Zhou, corresponding author of the paper, added, “This study underscores that psychosis is not a sudden event but a progressive process reflected in the brain’s communication networks. Individuals at high clinical risk already show distinctive patterns of reduced integration and local efficiency. Understanding these patterns gives us an opportunity to identify at-risk individuals earlier and with greater precision. Ultimately, integrating such imaging-based insights into clinical assessment could improve prognosis and allow for timely and preventive therapies.” Assoc Prof Zhou is also a Principal Investigator at the Centre for Sleep and Cognition, NUS Medicine.

Other collaborators of the study include Dr Maria Jalbrzikowski and Dr Dennis Hernaus, who chair the ENIGMA-CHR working group. Dr Jalbrzikowski is from the Department of Psychiatry and Behavioural Sciences, Boston Children’s Hospital, United States of America, and Dr Hernaus is from the Department of Psychiatry and Neuropsychology, Mental Health and Neuroscience Research Institute, Faculty of Health Medicine and Life Sciences, Maastricht University, Maastricht, the Netherlands.

“This study represents a significant step forward in understanding the biological trajectory of psychosis,” said Assoc Prof Lee. “By examining nearly 3,000 young people across multiple sites, we now have robust evidence that brain network disruption follows predictable patterns years before clinical symptoms fully emerge. This isn’t about finding a single faulty brain region, but understanding how the brain’s systems gradually become less coordinated, which opens a crucial window for early intervention that we’ve never had before. Being able to identify possible onset of psychosis early would allow us to intervene before symptoms take hold, improve long-term outcomes and reduce the impact of psychosis on young people’s lives.”

The study also suggests that the brains of young people at high risk for psychosis may be more vulnerable to certain types of damage, as observed in the reduced local backup connections and longer route between distant regions in the study. Young people at high risk for psychosis often face social difficulties, additional mental health issues, and a lower quality of life, creating a significant burden on them.¹ Preventive interventions could help ease this burden and possibly reduce the risk of progressing into fully developed psychosis.

The study enhances understanding of how psychosis may develop through interconnected brain pathways, supporting the hypothesis that tissue damage can spread across these networks. This underscores the importance of studying brain organisation to better trace the disease process. Building on these findings, the researchers plan to explore brain network patterns further with the goal of identifying biomarkers that could eventually support early detection and targeted interventions to lessen the long-term impact of psychosis.

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¹ <https://www.healthhub.sg/programmes/mindsg/caring-for-ourselves/understanding-psychosis-youths#psychosis-container>

About National University of Singapore (NUS)

The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research, and entrepreneurship, with a focus on Asian perspectives and expertise. We have 15 colleges, faculties, and schools across three campuses in Singapore, with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established more than 20 NUS Overseas Colleges entrepreneurial hubs around the world.

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, research centres of excellence, corporate labs and more than 30 university-level research institutes 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.

For more information on NUS, please visit <http://www.nus.edu.sg/>

About the NUS Yong Loo Lin School of Medicine (NUS Medicine)

The NUS Yong Loo Lin School of Medicine is Singapore's first and largest medical school. Our enduring mission centres on nurturing highly competent, values-driven, and inspired healthcare professionals to transform the practice of medicine and improve health around the world.

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 one of the leading medical schools in Asia and ranks among the best in the world (Times Higher Education World University Rankings 2025 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2025).

For more information about NUS Medicine, please visit <https://medicine.nus.edu.sg/>

About the Institute of Mental Health (IMH)

The Institute of Mental Health (IMH), a member of NHG Health, is the only tertiary psychiatric care institution in Singapore. Located on the sprawling 23-hectare campus of Buangkok Green Medical Park in the north-eastern part of Singapore, IMH offers a multidisciplinary and comprehensive range of psychiatric, rehabilitative and therapy services in hospital-based and community-based settings. The 2,000-bedded hospital aims to meet the needs of three groups of patients – children and adolescents (aged below 19 years), adults and the elderly. Besides providing clinical services, IMH dedicates resources to carry out mental health promotion and raise mental health literacy. IMH also leads in mental health research and training the next generation of mental health professionals in Singapore. For more information, please visit www.imh.com.sg.

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The NMRC was established in 1994 to oversee research funding from the Ministry of Health and support the development and advancement of biomedical research in Singapore, particularly in the public healthcare clusters and medical schools. NMRC engages in research strategy and planning, provides funding to support competitive research grants and core research enablers, and is responsible for the development of clinician scientists through awards and fellowships. The council's work is supported by the NMRC Office which is part of MOH Holdings Pte Ltd. Through its management of the various funding initiatives, NMRC promotes healthcare research in Singapore, for better health and economic outcomes.

About the National Research Foundation (NRF)

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