A HUB FOR BRAIN SCIENCE

With a strong foundation in neuroscience and clinical research, SHANGHAI IS INVESTING HEAVILY TO SPEARHEAD BRAIN RESEARCH, and forming a comprehensive network.

Two cloned macaque monkeys were born in late 2017 at the Institute of Neuroscience (ION) of the Chinese Academy of Sciences (CAS) in Shanghai. Created through somatic cell nuclear transfer, the same technique used to produce Dolly the sheep, they are the first cloned primates. This technology can yield genetically identical monkeys for animal models to study human brain diseases, said Mu-ming Poo, the ION director.

Just a year later, a gene-edited monkey was cloned at ION, leading to five identical monkeys sharing a gene mutation that interrupts the sleep cycle. These allow unprecedented exploration of neural mechanisms underlying sleep disorders and identifying diagnostic markers. Fewer animals are needed for testing as effects caused by genetic variation can be eliminated, according to Poo. His next step is to create models of brain disorders using cloned monkeys.

The roadmap for brain research

Developing effective diagnostic approaches and interventions for brain disorders is just one application of neuroscience studies in Poo's blueprint for China's brain science initiative — another is brain-machine intelligence technologies. These expanded technologies are all grounded on an improved understanding of the neural basis of cognitive functions, which is the main thrust of neuroscience research at ION, Poo explained.

This blueprint sets a roadmap for the development of brain research in Shanghai, which has also encompassed studies on the mental development of children and adolescents, with potential to inform innovative education models. With the increasing priority on brain research globally, Shanghai is determined to boost its capacity and expand its network in this field.

Its development plan is based on the city's traditional strengths in neuroscience and clinical research. "China's neuroscience research originates from studies on neurophysiology, led by the Shanghai Institute of Physiology at CAS," said Xiongli Yang, former director of the institute, and a CAS member from Fudan University. "From there, came the Shanghai Institute of Brain Research of CAS, ION's predecessor."

With pioneering work on the structure and function of the central nervous system, along with rich medical research resources, Shanghai has found its edge in neuroscience by integrating basic science and clinical studies, Yang said. An example is Fudan's State Key Laboratory of Medical Neurobiology, China's first national key laboratory in the field, which led a national major project exploring the associations between brain functions and major brain diseases. Its recent advances in the mechanisms of drug addiction and reward processing also hold valuable clinical potential.

Extensions of brain science

Interdisciplinary brain research centred on disease is a focus of Shanghai Jiaotong University (SJTU) School of Medicine. At its affiliated Ruijin Hospital, a cohort survey of 150,000 elderly people, the largest study of its kind in China, provides rich data for studies on Parkinson's and dementia, including pathogenesis and development. The studies have identified several factors for improving diagnosis of neurodegenerative diseases. With one of the world's largest deep brain stimulation treatment centres, the hospital also specializes in neuromodulation intervention for debilitating neurological symptoms, particularly in people with Parkinson's disease.

In line with the city's planning, technology platforms on basic neurobiology, brain diseases, and AI-assisted medical imaging are constructed at SJTU to link basic and clinical studies, as well as industrial application. Its Shanghai Mental Health Center directly supports drug development, having led more than 20 clinical drug studies in the past 30 years, including trials for a drug treating Alzheimer's disease.

Working with relevant research institutions, the Shanghai municipal government launched a major project for translational research to build brain-inspired algorithms and AI chips, supporting the development of machine intelligence and intelligent decision-making technologies. The project will also support research infrastructure building, by constructing Asia's largest brain imaging centre, which will support basic and clinical research on brain disorders, according to Jianfeng Feng, dean of the Institute of Science and Technology for Brain-Inspired Intelligence in Fudan University, a project leader.

Feng's team has also made progress in developing intelligent algorithms, and accumulated strong data for further progress in brain-inspired technologies.

"A challenge now is to use computational neuroscience to analyse the massive data and decode how the brain processes information, so that we can simulate the mechanism and develop brain-inspired algorithms using reverse engineering," said Feng. Yang also acknowledged that true integration of brain science and AI is a challenge. "Government support for big computation facilities and brain-inspired experiment platforms will help address this," Feng said.

Exploring the mechanisms of neural and cognitive development will also help provide a clearer picture of children's developmental trajectories. Seeing the educational potential of this research, a research team at East China Normal University, funded by the Science and Technology Commission of Shanghai Municipality (STCSM), launched a project in 2019 tracking brain development of 500 six-year-olds. Using advanced imaging and gene sequencing technologies, coupled with behavioural tracking and cognitive appraisal approaches, the project aims to build a multidimensional database on brain development of school-age children. "By exploring genetic, environmental, psychological and behavioural factors influencing children's brain development, we can improve our understanding of cognitive functions and build theoretical basis for novel education models," said Longnian Lin, a key player of the project.

Grounded on the basics

At the core of brain research is basic study on the neural networks and their functions. Another major science and technology project by the Shanghai municipal government will explore mesoscopic connectome, a step towards mapping all the connections in the brain. Structural and functional studies on the mesoscopic brain connectome are essential for understanding circuit mechanisms underlying higher cognitive functions and brain disorders, said Poo. Starting from zebra fish, the project, led by Poo's team, aims to accomplish mapping the mouse brain by 2025, and macaque monkey by 2030. Characterization of neuronal subtypes, cell type-specific connectivity and neural circuit analysis of brain functions are already underway.

Given its vast importance, the project is scaling up into an international collaboration. "We are keen to support such a platform for global collaboration," said Yang Song from STCSM. "This is in line with our plan to make Shanghai a global centre of science and technology innovation, and will further boost our research capacities in brain sciences." ■

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Zhongzhong is one of the first monkey clones created at Shanghai-based Institute of Neuroscience, CAS

The Shanghai Supercomputer Center provides technical support for the development of brain-inspired computation.

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Doctors at Ruijin Hospital implanting electrodes for deep brain stimulation.

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