# Brain science and technology: initiatives in the Shanghai and Yangtze River Delta region

**AUTHORS**
Xu Zhang[*], Qiang Zhang[†], Ying Mao[‡], Songtao Lv[‡], Qiang He[†], Dinggang Shen[†], Feng Shi[†] & Fangxiong Zhang[*]

**AFFILIATION**
[*]Institute of Brain-Intelligence Technology, Zhangjiang Lab; Shanghai Research Center for Brain Science and Brain-Inspired Intelligence, Building No. 12, 100 Haike Road, Zhangjiang Science City, Pudong New Area, Shanghai City, P. R. China.
[†]United Imaging Healthcare Technology Group Co., Ltd., 2258 Chengbei Road, Jiading District, Shanghai City, P. R. China.
[‡]Neurosurgery Huashan Hospital, 12 Middle Road, Urumqi, Jing'an District, Shanghai City, P. R. China; the Tianqiao and Chrissy Chen Institute for Translational Research, 480 North Wulumuqi Road, Suite 1701, Shanghai 200040, P. R. China.
[‡]Shanghai Green Valley Pharmaceutical Co. Ltd., 421 Niudun Road, Zhangjiang Hi-Tech Park, Pudong New Area, Shanghai City, P. R. China.

With hundreds of billions of neurons and hundreds of trillions of synaptic connections, the human brain can be called one of the most complex biological systems in the natural world. It is the basis of human perception and intelligence. Research on the brain, including its structure and function, sits at the forefront of scientific and technological exploration. With the new generation of artificial intelligence (AI) technology, industrial demands are driving further exploration of the human brain's cognitive neural mechanisms, and its integration with brain-inspired intelligence technologies — intelligent technologies with development inspired by brain and neuroscience principles.

Many nations, including the United States, European Union and Japan, have launched brain research programmes. Billions of dollars of investment globally have led to hundreds of publications reporting breakthroughs in brain cell typing, neural circuit analysis, neural activity recording, brain function intervention, theoretical and data analysis tools, human neurobiology and cross-integration technologies. However, gaps remain in understanding, from cognitive function to ageing and pathology. Further breakthroughs in brain-inspired computing systems and devices will require a deeper understanding of the neural mechanisms of the brain.

China announced in 2016 the launch of its Brain Science and Brain-Inspired Intelligence Project to explore the neurological basis of human cognition, while informing the treatment of brain diseases and advancing brain-inspired intelligence and computing technologies. Cities like Shanghai soon started investing in brain-inspired intelligence research to support the development of relevant industries. The Institute of Brain-Intelligence Technology (BIT) was established at the Zhangjiang Lab, built in Pudong's Zhangjiang Science City, in 2017, to promote interdisciplinary research on life science and information technology, positioning Shanghai as a globally influential science and technology innovation centre. The Shanghai Municipal Government established the Shanghai Research Center for Brain Science and Brain-Inspired Intelligence (Shanghai Brain/AI Center) in 2018 (**Fig. 1**). As an important unit of the Zhangjiang Lab, a national science centre and a brain technology centre in the Yangtze River Delta, the Shanghai Brain/AI Center provides research and technical support to national and local brain science and technology projects. Research areas include brain intelligence development, brain cognition disorders and brain-inspired computing based on artificial neural networks. It organizes major strategic projects in Shanghai and across southern China, including coordinating and managing joint research projects. It conducts strategic studies on brain science and brain-inspired intelligence technology, identifies research trends and proposes recommendations on directions for emerging, cross-disciplinary research. It assists in big science projects with international partnerships and promotes technology transfer with the Shanghai Center for Brain-Intelligence Engineering, a platform established in Pudong to promote research–industry partnerships in brain science.

**Figure 1: The Shanghai Research Center for Brain Science and Brain-Inspired Intelligence.**

The Shanghai Brain/AI Center organizes international conferences and joins relevant international projects to promote international collaboration. It mobilizes brain science and brain-inspired intelligence research resources of universities, research institutes, hospitals, and relevant enterprises in Shanghai, the Yangtze River Delta region and southern China. It is constructing a regional research network, with the Zhangjiang headquarters as the core. By pioneering a 'centre + node' model, it will play a central role in the research network, exploring mechanisms for open innovation.

An open and integrated mechanism supports cross-disciplinary research. Brain science, by nature, is interdisciplinary; brain-inspired intelligence is even more so, encompassing mathematics, information science, materials science and automation control. The Shanghai Brain/AI Center will collaborate with regional research institutes and universities to coordinate resources here and abroad, advancing brain science theories, diagnostic and treatment techniques for brain diseases, and AI technologies, while building a powerhouse for brain science and brain-inspired intelligence research.

The Shanghai Brain/AI Center will collaborate with the Institute of Neuroscience of the Chinese Academy of Sciences (CAS), the Huazhong University of Science and Technology (HUST)-Suzhou Institute for Brainsmatics, and the Kunming Institute of Zoology of CAS to research the mechanisms of perception and cognition. Work with United Imaging Healthcare (United Imaging), a Shanghai-based medical technology company, will map the structure and functions of the human brain for a functional atlas. Projects with the Huashan Hospital of Fudan University, the Shanghai Mental Health Center of Shanghai Jiao Tong University, and the Second Affiliated Hospital of Zhejiang University School of Medicine will jointly explore the diagnostic and treatment strategies for neurodegenerative diseases, and support drug discovery via partnerships with research and development (R&D) institutions. Alliances with the Center for Brain Science and Education Innovation of East China Normal University, and Xinhua Hospital of Shanghai Jiao Tong University will explore the cognitive and psychological basis of brain development in children's education. In brain-inspired intelligence technology, the centre is establishing a collaborating research network with Zhejiang University's Frontier Science Center for Brain and Brain Integration, and Shanghai Jiao Tong University's Artificial Intelligence Institute, and utilizes the platform of the Shanghai Center for Brain-Intelligence Engineering to promote collaboration with enterprises for the development and application of AI engineering technologies.

Through collaborations, the Shanghai Brain/AI Center will gradually build public technology platforms for human brain mapping, neural network structures and functions, clinical research into brain functions and brain diseases, neural network computing and information technology, intelligent perception and cognition, and brain information databases.

## IMAGING TECHNOLOGIES FOR EXPLORING BRAIN STRUCTURE AND FUNCTION

Medical imaging technology is important for observing the internal structure of the human brain and obtaining macro- and micro-level information. Rapid recent developments, including magnetic resonance imaging (MRI), positron emission tomography (PET) or PET/computed tomography (CT), and integrated PET/MRI, have illuminated brain structure, functions and molecular metabolism, providing rigorous technical support to further investigation.

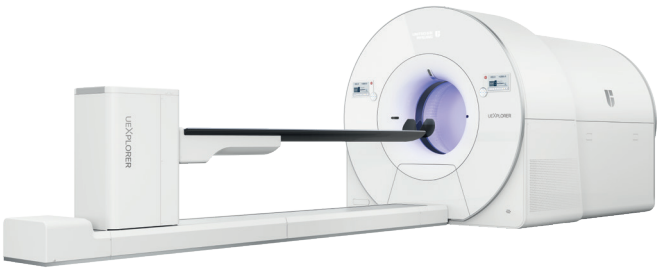

**Figure 2: United Imaging's total-body PET/CT uEXPLORER.** *United Imaging Healthcare Technology Group Co., Ltd.*

The Molecular and Functional Atlas of the Chinese Brain, initiated by Zhangjiang Lab's BIT, is applying advanced imaging equipment and techniques to frontier brain-mapping studies. It is organized by Shanghai-based United Imaging, which has a full portfolio of advanced medical imaging and radiotherapy products, as well as innovative medical IT and AI solutions, and brings together Shanghai Jiao Tong University, Huashan Hospital (West Campus) of Fudan University, and other top-tier domestic research institutes and hospitals. The goal is to map the molecular and functional brain regions and their connectome over the life of healthy brains, focusing on the effects of differences in language, education and living environment, and to reveal the key functional connectome of perception and cognition, and its laws of development and ageing. It will attempt to identify changes in brain areas and their connectome in those with autism, intellectual disability, depression, and neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD). Using the functional connectome big data, computational neuroscientists will build theoretical models of perception and cognition, to establish a basis for developing a simulated brain, and the corresponding AI algorithms and hardware.

The project uses United Imaging's advanced imaging equipment, including the research dedicated high-performance 3.0T MR, high definition (HD) time-of-flight (TOF) PET/MR, and the world's first total-body PET/CT, 'uEXPLORER' (**Fig. 2**), to construct a high-resolution, high-reliability brain atlas.

The research dedicated high-performance 3.0T MR can provide quality and efficiency beyond those of conventional imaging, and achieve dynamic and static imaging quickly and accurately, with full-sequence coverage for the whole body. Precise tracking of white-matter fiber can detect brain dynamics in multiple dimensions, facilitating the study of cognitive and neural connections.
The project also introduced Quantitative Susceptibility Mapping (QSM),[1] which can quantitatively reveal tissue susceptibility related biomarkers in various brain diseases, such as deep brain iron deposition in AD/multiple sclerosis (MS)/PD,[2–4] venous oxygen saturation disturbance in stroke,[5] and cancer haemorrhage/calcification

as a result of chemotherapy,[6] potentially improving understanding of the pathogenic mechanisms.

HD TOF PET/MR can achieve rapid synchronous dynamic imaging of endogenous/exogenous brain metabolism, to efficiently integrate multimodal brain metabolic image information, and to establish a comprehensive brain metabolism map that provides important molecular targets for clinical research on brain diseases.

uEXPLORER has a 194-cm axial PET field of view (FOV) that enables a whole-body scan to be completed at one bed position, with significantly improved system sensitivity and an ultra-low patient dose (**Fig. 2**). Its unique four-dimensional real-time whole-body dynamic imaging has made it possible to clearly visualize the entire process of injected drugs flowing, diffusing and becoming metabolized in blood vessels.

The project will also develop ultra-fast three-dimensional magnetic resonance spectroscopic imaging (MRSI),[7–14] a unique method of unlabelled molecular imaging, which can provide more accurate quantification of challenging neurotransmitters, such as glutamate and GABA[15], as well as simultaneously generating multimodal contrasts from multiple brain metabolites[16,17] from a single acquisition. This will be critical in our quest to answer fundamental questions in areas such as early brain development, psychiatric disorders and neurodegenerative diseases.

United Imaging will apply AI technology to construct a more accurate brain atlas and promote associated research. Based on image data from collaborating organizations, United Imaging's big data intelligent platform will use novel analysis models for online processing of multi-modal image data. Advanced intelligent algorithms will enable faster and more accurate calculation. It also promises open technology platforms to facilitate the interface between the brain atlas and other platforms and databases, including a clinical intelligent diagnosis platform, education database and drug-development database, supporting secondary development of the brain atlas and data sharing.

## PROGRESS IN BRAIN DISEASE RESEARCH

The study of brain structure and function is the basis for exploring the causes and treatment of brain diseases. The Molecular and Functional Atlas of the Chinese Brain is mapping brain regions and the connectome in human and animal disease models, to achieve research breakthroughs. This should facilitate the development of drug and treatment technologies, and the exploration of children's psychological development and mental health.

## NEW DRUGS FOR ALZHEIMER'S DISEASE

Today's understanding of brain diseases is not limited to local brain lesions caused by abnormal neurological functions of individual genes or proteins; rather, it extends to disorders in whole body systems. Examples could be the increasing number of reports on the crucial role of gut microbiota imbalances in brain diseases like AD, PD and depression, which offered a novel perspective for designing treatment strategies.

The world's first oligosaccharide drug for AD, GV-971, was jointly developed by the Green Valley Pharmaceutical, which houses a joint facility with the Zhangjiang Lab, Ocean University of China and Shanghai Institute of Materia Medica (SIMM) under the CAS. GV-971 achieved promising positive outcomes in a phase 3 clinical trial, improving cognitive impairment among patients with mild-to-moderate AD. It may combat AD by reconditioning gut microbiota, therapeutically harnessing gut bacterial amino acid-influenced neuroinflammation and inhibiting amyloid-beta peptide (**Fig. 3**).

Exploring the diagnosis and treatment of brain diseases is on the agenda of Shanghai's blueprint of brain science development. Green Valley will use GV-971 to launch a 'Brain • Health Project', focusing on AD and PD, which mainly affect the elderly. This will systematically illuminate the crosstalk among multiple body systems and reveal their evolutionary mechanisms as a common pathological basis in major brain diseases. Researchers will develop biomarker and target groups based on the common pathological mechanisms, and design preventive measures, early diagnosis methods and systematic intervention strategies, with the aim of developing long-term health management plans and effective treatments.

The project will build standardized national cohort studies of brain diseases based on international standards, and bio-sample libraries and databases of the Chinese population. Through collaboration with brain science experts and research institutions from home and abroad, including the Shanghai Brain/AI Center, Green Valley will employ AI technology to conduct in-depth data mining and analysis, via big data modelling and optimization. Results will guide the development of a series of early diagnosis markers, drugs and non-pharmaceutical treatment interventions, in the hope of creating a precision brain diagnosis and treatment platform at Green Valley with integrated clinical, research, information and industry components, and implementing a data-driven innovation system for brain research.


**Figure 3: GV-971 has shown promise in clinical trials as a novel oligosaccharide drug targeting gut-brain axis.** *Shanghai Green Valley Pharmaceutical Co. Ltd.*

## NOVEL TECHNOLOGIES FOR TREATING BRAIN DISEASES

Novel technologies are also playing important roles in the treatment of brain diseases. One research priority of the Shanghai-based Tianqiao and Chrissy Chen Institute (TCCI) for Translational Research is using electronic games to assistant in diagnosis and treatment.

The renowned brain science research organization and the Shanghai Zhou Liangfu Medical Development Foundation established the TCCI for Translational Research with a 500 million RMB investment. The institute has partnered with Huashan Hospital of Fudan University and the Shanghai Mental Health Center to focus on translational research on digital drugs that assist the evaluation, diagnosis and treatment of brain diseases. They are bringing together outstanding neurological and psychiatric researchers, and aggregating private capital to create a sustainable development model. The institute is committed

**Figure 4: Tianqiao and Chrissy Chen Institute Clinical Translational Research Center.**

to funding frontier research abroad, bridging downstream and upstream research in China, and promoting translational brain disease research worldwide (**Fig. 4**).

The first original brain disease research funded by the institute is developing virtual reality (VR) games, led by Huashan Hospital doctors, to assist the evaluation and treatment of dementia among the elderly. This cognitive training and evaluation system can simulate many real-world scenarios with remarkable precision. By completing tasks, like shopping, in VR, elderly users will receive stimulation training for multiple cognitive functions, such as attention and memory, as well as computing skills. Their behaviours in the game, including eye movements, reactions and walking routes, will be recorded and analysed to serve as an indicator for cognitive assessment.

The product avoids the drawbacks of traditional cognitive evaluation methods, such as inefficiency, boredom and low participation rate, establishing a system of early screening and early intervention for cognitive impairment among the elderly. The phase 1 product has already entered communities in Shanghai, and is showing good results in trials among the elderly. Working with game companies to improve the design, the TCCI for Translational Research is actively promoting phase 2 research and clinical trials of the project.

The centre is cooperating with renowned overseas universities and research institutions to introduce cutting-edge technologies and products to China, including cell phone, TV, and motion-sensing games that have shown positive effects in treating attention deficit hyperactivity disorder (ADHD) among children, anxiety among the young, and old-age cognitive disorders. The institute is actively introducing digital drug products, including online software for self-administered mental health assessment and suicide prediction. Working with Chinese hospitals, it is developing the Chinese version of these products for the benefit of patients.

The TCCI for Translational Research utilizes the research capacity and clinical resources of Huashan Hospital (West Campus) in neurology. With 800 beds, nearly 300 physicians and 400 nurses, it is one of the world's busiest medical centres in neurology: it conducted 1,500 surgeries monthly in the first year of its opening. As a research hospital, it has lab space of more than 10,000 square metres, 50 beds for clinical trials, and large databases from brain disease cohort studies and brain banks. It has also developed a multi-functional, high-density, ultra-flexible cortical electrode for collecting high-quality electrocorticogram signals. Using silk protein as the substrate, the electrode is ultrathin and can be attached to the brain cortex, enabling more accurate locating of brain wave transmission pathways. Used together with drugs, such as anti-epilepsy drugs, it can monitor and enhance their effects.

Huashan Hospital's partnership with the TCCI has helped to connect basic research with clinical use, accelerating the translation of research like the cortical electrode, which is now at the commercialization stage. This has made Huashan Hospital a medical centre for brain research in southern China.

## CHILDHOOD MENTAL HEALTH RESEARCH

The clinical application of brain science includes mental health, especially its improvement and education in children, through the exploration of neurodevelopment and cognitive psychology. The Shanghai Brain/AI Center actively cooperates with medical and research institutions to promote cross-disciplinary research in neuroscience, psychology and medicine. The study of the mental health of children and adolescents is also on the agenda of the Molecular and Functional Atlas of the Chinese Brain.

Mapping brain development from infancy to adulthood could provide detailed data and a theoretical basis for interpreting the effects of lifestyle, cultural background and educational environment on the structure and function of the brain, and imaging the molecular state. By establishing brain maps, the project might help families and educational institutions establish a personalized teaching system based on the understanding of cognition science.

Molecular and functional brain maps of the infant and adolescent stages might be used to establish associations with intellectual disability, learning difficulties and emotional behaviours, to guide and optimize intervention and education methods. United Imaging is exploring the concept of a childhood brain development curve akin to those for height and weight.

## FROM BRAIN-INSPIRED COMPUTING TO BRAIN SCIENCE AND TECHNOLOGY DEVELOPMENT

Brain-inspired intelligence technology is an important part of the China Brain Project and the development plan for Shanghai's brain science. Zhangjiang Lab's BIT and the Shanghai Brain/AI Center are collaborating with iFLYTEK and other high-tech companies to promote the development of brain-inspired intelligence research.

In the 2019 Scholastic Achievement Test (SAT) Math Question Answering competition organized by the International Workshop on Semantic Evaluation, a joint team from the Shanghai Brain/AI Center and iFLYTEK defeated 132 other groups and earned the highest total score. They utilized the new mathematical theory of assertion logic proposed by Zhou Yi from BIT, which facilitated the deep reasoning ability of AI. iFLYTEK, with its strong engineering implementation capability, provided important technical support.

The crossover cooperation between the Shanghai Brain/AI Center, Zhangjiang Lab's BIT and the IT industry is also embodied in Cambricon, a world leading

smart-chip provider that joined forces with the Shanghai Center for Brain-Intelligence Engineering to explore the commercialization of brain-inspired intelligence research.

Cambricon is a pioneer in the design and production of processor and computer chips for AI and machine-learning applications (**Fig. 5**). Its vision is to make machines that better understand and serve people and society. Its core members all came from top Chinese universities, with rich research and technical backgrounds in AI.

In 2016, when Cambricon was founded, it released Cambricon-1A, a processor specialized for deep learning, with high performance and energy efficiency. Benefiting from its highly specialized hardware architecture, the processor could maximize its performance in machine-learning applications, such as computer vision, voice recognition and nature language processing.

The following year, it released Cambricon-1H8 and Cambricon-1H16: the former has a smaller footprint and lower power consumption than its predecessor (Cambricon-1A), and can be used in computer vision applications such as surveillance cameras and autonomous driving; the latter has significantly improved the energy efficiency.

Development of these chips is based on deep neural networks, a prevalent algorithmic model in the field of machine learning. Its establishment was inspired by the connection mode of the neural network in the human brain and abstracted from the perspective of information processing. Cooperation with researchers in basic neuroscience on mapping the brain function connectome might further inspire AI scientists in developing smart chips.

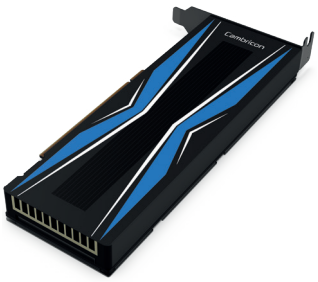


**Figure 5: Cambricon develops innovative smart chip technology.**
*Cambricon Technologies Corporation*

Since the artificial neural network computing model can be optimized at the hardware level, new processor architecture will likely bring about performance improvements. Smart chips developed by Cambricon are used in smart phones and various embedded devices. The company has established strong working relationships with upstream and downstream enterprises in the information industry.

Cambricon has developed complete lines of smart chips and processing cards. Its Machine Learning Unit (MLU) is designed to accelerate the machine learning inference on the server side, with orders of magnitude improvements in speed and power efficiency. Its MLU100 machine learning processor chip (**Fig. 5**), introduced in 2018, provides powerful computing support for AI inference. This relatively versatile processor can support multiple deep learning techniques, as well as multi-mode intelligent processing including visual, speech, natural language and a range of applications. Through cooperation with Zhangjiang Lab's BIT, both parties are expected to achieve breakthroughs in AI algorithms, and to develop more intelligent chips and technologies in future.

## BUILDING A FLOURISHING FUTURE

These brain science and technology initiatives are expansive and growing. Zhangjiang Lab's BIT and the Shanghai Brain/AI Center plan to build a brain science database and information hub, promoting data sharing among projects and organizations, to support the integration and application of resources for scientific research projects. Through this open cooperation model, the basic research results of brain science will be transferred and applied in the clinical and AI industries more rapidly. We look forward to accelerating the integration of inter-disciplinary and cross-disciplinary innovations to achieve high-level scientific research and technological innovation, and to promote the development of brain science and brain-inspired intelligence research in Shanghai and across China as a whole.

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