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The first International Life Science Summer Summit (Beidaihe)

ENHANCING BRAIN HEALTH WITH SCIENCE

The human brain is probably the most astonishing of the body´s organs and its workings have intrigued scientists throughout history. The major endeavours in neuroscience now are mapping neuron activities to understand the cognitive processes, driving technologies for artificial intelligence and developing therapies for brain disorders. Many countries and regions, such as the United States, Japan and Europe have made huge investments and China is expected to soon launch its own brain project to catch up with the world.

Focusing on brain science and health, the first International Life Science Summer Summit held recently in Beidaihe drew many world-renowned neuroscience experts and clinicians to promote interdisciplinary exchange and collaboration, in support of the development of China Brain Project.

From brain research to brain health

"Brain science is one of the most challenging frontier areas," said Shumin Duan, dean of the School of Medicine, Zhejiang University. "It explores the neural basis of consciousness, and even touches the fundamentals of philosophy." Duan said that while there is a macro-level understanding of the brain, knowledge about how the neural circuitry works is still very limited. Integrating studies of neural circuitry with the exploration of artificial intelligence requires greater support for interdisciplinary collaboration. Also, an impetus to improve understanding is building as increased longevity, and growing social pressures, bring greater incidence of brain diseases, such as stroke, dementia and various psychiatric disorders.

Duan sees great opportunities for the development of brain sciences in China. Burgeoning techniques, such as optogenetics and neuroimaging, have led to important breakthroughs, enabling the classification, tracking and control of neurons, and the visualization of functioning neural circuitry. In China, steady funding increases, along with various plans to lure talent, have boosted the number of neuroscience researchers, paving the way for research growth.

Duan´s ideas were echoed by clinicians. Liwei Zhang, vice director of Beijing´s Tiantan Hospital, and Ying Mao, vice director of the Huashan Hospital in Shanghai both emphasized how neuroimaging promoted the development of diagnosis and treatment of brain diseases. "Imaging technology is the cornerstone for the development of neurosurgery," said Zhang. "It enables minimally invasive brain surgery." Functional imaging also assists the development of brain-computer interfaces (BCI), which is an exciting area to explore, according to Mao.

Using the multimode neuroimaging technique, Tianzi Jiang from the Institute of Automation, Chinese Academy of Sciences, developed a full brain atlas based on connectivity profiles-the brainnetome atlas. "It brings us insight into the brain function and the pathophysiological mechanism of psychiatric and neurological disorders," said Jiang. "It assists with early diagnosis and precise treatment."

Optical and photonic techniques, genetic tools and other technological breakthroughs have yielded results in the United States, where the Brain Initiative has been running for five years, according to Richard Huganir, director of the Kavli Neuroscience Discovery Institute at Johns Hopkins University. Priority areas for the initiative include techniques to monitor neural activity and identify cell types, tools for circuit diagrams and precise intervention, advancement of human neuroscience, theory and data analysis tools, as well as the integration of all these approaches. Analysis of the large amounts of data generated by these advanced tools presents a big challenge, Huganir explained.

Peter Bootsma, Counsellor of Health, Welfare and Sports from the Netherlands embassy introduced policies on dementia research in the Netherlands. He highlighted the need for research on prevention and cure to enable timely diagnosis and integrated care. Central to the Dutch government´s policies are social innovations in long-term care, aiming at improving patients' quality of life.

Neurodegenerative diseases

The value of early diagnosis of Alzheimer´s disease (AD) was underlined by Zhenxin Zhang, chairman of the scientific committee from the National Clinical Research Centre of Neurological Diseases. Zhang led a genome-wide single variant association study for AD. Applying genetic screening tests and comprehensive checks, she found significant increases in the prevalence of AD in China, prompting calls for standardized examination and enhanced clinical research to develop novel AD drugs.

In support of early diagnosis, the BIOCARD study, a population-based clinical research led by Marilyn Albert, director of the cognitive neuroscience division at Johns Hopkins University, seeks to identify biomarkers of cognitive decline among normal individuals. Focusing on AD, the study employed cognitive testing, MRI, cerebrospinal fluid (CSF) and blood tests, to collect panel data on cognitive changes. The results suggested that cognitive test scores correlated with symptom progression, and that the risk of cognitive decline was doubled among those with an ApoE-4, a protein that carries cholesterol to neurons. MRI scans also identified medial temporal lobe deformation during preclinical AD. "It´s an extraordinary dataset that generates multiple findings and can be used for many other things," said Albert. "We look forward to expanding our understanding of risk factors and improving design of clinical studies for novel therapies."

In an overview of the US clinical trial network infrastructure for AD, Howard Feldman from the University of California, San Diego, suggested focusing on target selection and innovative trial design. As the director of the Alzheimer´s Disease Cooperative Study, a public-private partnership to test novel treatments and prevention for AD, Feldman introduced the landscape of AD drug development. The 30 new therapies in early clinical testing now cover three diverse classes of drug targets, 45% of them amyloid-based. However, Feldman said, society is "starved" of treatments for AD, as many trials fail at phase 1. He urged further development of the pipeline, advanced designs and methods, and rigorous Proof of Concept (POC) in phase 2, as well as simplifying phase 3 confirmatory trials.

Identification of new drug targets requires basic studies of proteins to explore the molecular, cellular and genetic mechanisms of neurodegenerative diseases. Cell biologists, Rong Li, from Johns Hopkins University reported that mitochondria, organelles that power the cells, also help remove aggregated proteins. "We call it MAGIC-mitochondria as guardian in cytosol," said Li. "It´s a system for disposing intra-cellular wastes." Yet, too many misfoldedproteins will lead to mitochondria damage. "Our study provides a link between mitochondria dysfunction and protein aggregation, caused by cell stress," said Li. "The research could lead to brand new therapeutic targets for neurodegeneration."

Virginia Lee from the University of Pennsylvania discussed the transmission of α-synuclein, which is shown as a potential mechanism of Parkinson´s disease (PD) pathogenesis. Intracellular oligodendrocyte environment converts misfolded α-synuclein into a GCI-like strain. "By targeting the misfolded proteins, we can block their transfer to neighbouring cells," said Lee.

Bai Lu from Tsinghua University is focused on the brain-derived neurotrophic factor, or BDNF, for drug discovery for neurodegenerative diseases. Targeting synaptic repair, he reports that the TrkB agonist antibody activates the BDNF pathway. The study suggests therapeutic potential of TrkB agonists, said Lu.

Neuromodulation, with the development of deep brain stimulation (DBS) technology, provides another treatment option for neurosurgeons. But, for motor neurone disease patients, or those with spinal cord injuries, BCI technology presents an exciting alternative to regain lost functions. "Neurons in the motor cortex encode movement direction," said Bo Hong, a biomedical engineer from Tsinghua University. "Based on that, we can createa BCI that allows patients to control the mouse cursor." To lower the risk of infection caused by electrode implants, Hong´s team demonstrated the feasibility of a minimally invasive BCI using electroencephalographic activity recorded from above the dura matter, with fewer electrodes reducing the system complexity. "Our next step is to invent a BCI that turns thoughts directly into speech," said Hong.

Tackling neurodegenerative diseases is a multi-level issue. "By providing a platform for cross-disciplinary dialogue," said Jianpei Xu, vice governor of Hebei province, "we can promote innovation in the health industry." ■

Mayor Zhang Ruishu introducing the Beidaihe(BDH) Life Science and Healthcare Innovation Demonstration Zone at the conference

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