


2019 Academic Annual Meeting and the Frontier Seminar on “Glial Cell Function and Disease” (Nantong, China)

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Abstract

The contribution of glial activities to the functions, diseases, and repair of the central nervous system has received increasing attention in neuroscience studies. To promote the research of glial cells and increase cooperation with peers, the 2019 Academic Annual Meeting and the Frontier Seminar on “Glial Cell Function and Disease” was held in Nantong City, Jiangsu Province, China from May 24 to 26. The meeting was organized by Drs. Yong-Jing Gao and Jia-Wei Zhou of the Chinese Society of Neuroscience Glia Branch. The conference focused on the physiological and pathological functions of astrocytes, microglia, and oligodendrocytes with 25 speakers in two plenary speeches and five sections of more than 180 participants engaged in glial cell research. In the two plenary lectures, Yutian Wang from the University of British Columbia and Xia Zhang from the University of Ottawa presented “Development of NMDAR (N-methyl-D-aspartic acid receptor)-positive allosteric modulators as novel therapeutics for brain disorders” and “Mechanisms underlying cannabinoid regulation of brain function and disease,” respectively. The five sections included microglia and disease, astrocytes and disease, glioma treatment and glial imaging, oligodendrocytes and disease, and glial–neuronal interactions and disease. This meeting allowed extensive and in-depth academic exchanges on the latest research and experimental techniques, represented the highest achievements of Chinese scholars on glial cells, and promoted the cooperation between peers in the fields of glia studies.

Keywords

Chinese Society of Neuroscience Glia Branch, glial cells, function, mechanism, technology

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Increased attention to the role of glial activities in neural functions and diseases has drawn the participation of more than 180 experts who engaged in glial cell research to the 2019 Academic Annual Meeting and the Frontier Seminar on “Glial Cell Function and Disease” held in Nantong, China from May 24 to 26. The meeting was organized by Drs. Yong-Jing Gao and Jia-Wei Zhou of the Chinese Society of Neuroscience Glia Branch. The conference focused on the physiological and pathological functions of astrocytes, microglia, and oligodendrocytes presented by two plenary lectures and five sections presented by 25 speakers and others.

The meeting opened with the letters from Drs. Xiong-Li Yang and Shu-Min Duan, Honorary Chairmen of the Academic Committee, members of Chinese Academy of Sciences, which briefly reviewed the development of studies on Glial Cells and stated their expectation that the future of Chinese Brain Research Program would be in the hands of young generations of neuroscientists.

Plenary Speeches

In the first plenary lecture, Yutian Wang (University of British Columbia, Canada) began the academic exchanges with “Development of NMDAR (N-methyl-D-aspartic acid receptor)-positive allosteric modulators as novel therapeutics for brain disorders.” In this lecture, Dr. Wang systematically reviewed their contribution to the theoretical development of different subtypes of glutamate NMDAR in synaptic and extrasynaptic

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neurotransmissions. Then, he presented that in study on the involvement of NMDAR in stroke-evoked cell death, his team identified a series of specific and selective modulators of NMDAR subunits and highlighted the potential of using GluN2A-NMDAR-positive allosteric potentiators (Npams) to activate pro-survival signaling and reduce excitotoxic/ischemic neuronal injuries *in vitro* and *in vivo*. Interestingly, the protective effect of Npams was still viable used hours after the initial ischemia/reperfusion by dually intensifying long-term potentiation and long-term depression (Dalton et al., 2012; Yu et al., 2018). As extrasynaptic neurotransmissions are closely associated with astrocytic release of glutamate, their study opens a possibility to alleviate ischemic injury and other excitotoxic neural diseases, such as Alexander's disease and schizophrenia through specifically modulating astrocytic glutamate release.

The second plenary speaker Xia Zhang (University of Ottawa) presented "Mechanisms underlying cannabinoid regulation of brain function and disease." Therapeutic usage of cannabis has a history of more than 5,000 years in China. In recent 20 years, endogenous cannabis and cannabinoid receptors were also identified. Zhang's team has systematically studied the effect of cannabis on reward, memory, sleep, cognition, anxiety, and depression by using a variety of biotechniques, with specific interest in cannabinoid receptors that were present in astrocytes and microglia. Dr. Zhang specifically highlighted a top-down wake circuitry wherein increased activity of the medial prefrontal cortex could modulate the activity of well-established sleep-associated neuronal activity in the raphe nucleus, locus coeruleus, and ventral tegmental area. This finding has deepened our understanding of the mechanisms underlying sleep awakening in addition to the long-established ascending reticular activating system (Zhong et al., 2017).

Microglia and Disease

The first keynote speaker Yu-Qiu Zhang (Fudan University) presented "Involvement of hippocampal microglia in anxiodepressive-like behaviors induced by chronic pain." Dr. Zhang reported that at 14 days after chronic constriction injury of infraorbital nerve (COIN), both rats and mice exhibited anxiodepressive-like behaviors along with trigeminal neuralgia and microglia activation in the hippocampus. The results obtained by combined methods of animal behavioral observation, pharmacology, electrophysiology, optogenetics, and chemical genetics highlighted that hippocampal microglial activation mediates COIN-induced anxiodepressive-like behaviors in rodents. This behavioral change was correlated with hippocampal neuroinflammation mediated by ATP-gated P2X7 receptor-microglia-interleukin-1 β and indoleamine 2,3-dioxygenase metabolic

pathway (Chen et al., 2019). Subsequently, Yu Zhou (Qingdao University) presented "Microglia regulates contextual fear memory linking," Zhi-Hua Gao (Zhejiang University) presented "Regulation of microglia activity: a purinergic affair," and Bo Peng presented "Deciphering the origins of repopulated microglia in the central nervous system." The application of modern molecular biology and imaging techniques in these studies left a very living impression on the audience.

The last presenter in this section was Yong-Jing Gao (Nantong University) with the topic of "The association of nuclear factor of activated T-cells (NFAT1) regulation of spinal microglia proliferation after spinal nerve ligation with neuralgia." In this model, NFAT1 expression in spinal microglia was found under the regulation of DNA methylation by Tet methylcytosine dioxygenase 2 and Ca²⁺/calcineurin. NFAT1 knockout mice showed less microglia activation and reduced pathologic neuralgia. The latter effect was simulated by inhibition of microglia proliferation. These findings provided several potential targets for suppressing neuralgia (Zhang et al., 2017; Wu et al., 2019).

Astrocytes and Disease

The section was covered by three speakers led by Jia-Wei Zhou (Chinese Academy of Sciences, Shanghai). To reveal the contribution of astrocytes to neuroinflammation during the development of Parkinson's disease, Zhou's team has studied the role of Ebf1 (early B cell factor 1) and its downstream effector Rgs5 (regulator of G-protein signaling 5) in lipopolysaccharide-evoked pro-inflammatory activity around dopaminergic neurons. The results revealed that Ebf1/Rgs5 signaling axis was a critical determinant for astrocyte activation *in vivo*. This result was very helpful for designing novel therapies targeting the astrocyte-driven neuroinflammation and associated neurodegenerative diseases (Q. Li et al., 2019).

Jie Zhang (Xiamen University) and Yan Li (Xi'an Jiaotong University) then presented their talks entitled "Menin (Multiple endocrine neoplasia type 1) deficiency leads to depressive behavior by modulating astrocyte-mediated neuroinflammation" and "The reprogramming of astrocytic glycogen metabolism in ischemia-reperfusion injury," respectively. The former report was about the signaling process leading to astrocytic Menin (Multiple endocrine neoplasia type 1)-evoked neuroinflammation and the therapeutic potential of targeting Menin in major depressive disorder. The latter one revealed that decreased glycogenolysis was responsible for the excessive glycogen accumulation in astrocytes following ischemia/reperfusion, which reduced lactate supplement from astrocytes to neurons and caused tricarboxylic acid cycle disorder, thereby leading to neuronal death. This report also highlighted that glycogen

phosphorylase was a potential intervention target for ischemic stroke.

Glioma Treatment and Glial Imaging

As a critical step for the diagnosis and treatment of glioma, illuminating glioma cells was highlighted by neurosurgeons and experts of imaging technique development. Ying Mao (Shanghai Huanshan Hospital) and Wei Shi (Affiliated Hospital of Nantong University) presented their skills in manipulating glioma in and out of the operation rooms. Mao emphasized on “The breaking point in individualized diagnosis and treatment based on the understanding of glioma metabolism.” Surprisingly, based on the inherent association between isocitrate dehydrogenases mutation and glioma development, his team could classify the tumor and identify glioma and its margin within 31 min during the surgery with 100% success. This achievement gave them the confidence to effectively elongate the life of patients with glioma except Grade IV (Xu et al., 2019). Alternatively, Shi focused his studies on “Combination therapy mediated by glioma dual targeted delivery system constructed by OPPD (Pep22 polypeptide drug delivery system).” Dr. Shi demonstrated that the OPPD drug-loading system not only targeted glioma cells that overexpressed low-density lipoprotein receptor but also had dual therapeutic effect on the tumor by transporting chemotherapeutic drug doxocycline, a matrix metalloprotease inhibitor, into glioma and by generating thermal effect by near infrared radiation (Qian et al., 2018).

In association with many brain diseases, studies on the mechanisms underlying spreading depolarization during neuronal hyperexcitation called upon extensive attention of the audience. “Enhanced gliotransmission and neural synchrony after spreading depolarization” presented by Ning Zhou (Shanghai Tech University) highlighted that astrocyte-originated, NMDAR-dependent slow inward currents driven by IP₃ (inositol trisphosphate) receptor-mediated Ca²⁺ wave underlay spreading depolarization and low-frequency synchrony of hippocampal neurons. This work provided a new target to control stroke, migraine, and other spreading depolarization-associated neuropathy (Wu et al., 2017).

In this section, the latest advancements in the biotechniques and their applications in glial studies were also highlighted. Zhao-Fa Wu (Peking University, on behalf of Yulong Li) and Xiao-Chun Gu presented “Spying on purinergic transmission by constructing new genetically encoded G-protein coupled receptor activation based (GRAB) fluorescent sensors” and “Roles of multi-channel optic imaging in neurovascular coupling study,” respectively. The former presentation showed that the development of purinergic GRAB sensors provides critical genetically encoded imaging probes for

investigating purinergic transmission with molecular specificity. The latter exhibited a powerful tool of combining GCaMP (a genetically encoded calcium sensor) with model microscopic techniques, such as optical coherence tomography and multiple-wavelength spectroimaging and laser speckle contrast imaging, in studying the reactive features of astrocytes in the neurovascular unit.

Oligodendrocytes and Disease

Lan Xiao (the Third Military University), Liang Zhang (Xiamen University), Feng Mei (the Third Military University), and Zeng-Qiang Yuan (Chinese Academy of Sciences) focused on the cellular and molecular mechanisms underlying the functions of oligodendrocytes in the myelination and the potential targets promoting remyelination in disease. They, respectively, presented the “Impacts of connexin-mediated oligodendro-astrocytic network on oligodendroglia development and remyelination” (Niu et al., 2019), “Nucleoporin Seh1-A novel regulator of oligodendrocytes differentiation and myelination,” “Enhancing oligodendrocyte myelination rescues synaptic loss and improves functional recovery after chronic hypoxia” (Li et al., 2018), and “A novel m⁶A reader Prrc2a controls oligodendroglial specification and myelination.” Their findings had important reference value in the development of medicine while unveiling the complex inter- and intra-cellular regulatory processes in this less explored type of glial cells.

Glial-Neuronal Interactions and Disease

Yang Su (Jinan University) presented “Synergistic toxicity between neurons and astrocytes in the pathogenesis of spinocerebellar ataxia 17.” It showed that synergistic toxicity of mutant TATA (a conserved DNA promoter sequence enriched in TATAAA)-binding protein in neurons and astrocytes played a critical role in this ataxia (Yang et al., 2017). Gang Chen (Nantong University) addressed the “Roles of Schwann cells in the functional recovery of peripheral nerve injury” and identified lysosome-associated neuralgia and the signaling process. “Glia in addiction” was the topic of Tifei Yuan (Shanghai Mental Health Center), and it highlighted the contribution of glial transmission to the synaptic plasticity in addiction.

The end of the session came with the presentation of “Retinal Muller cell gliosis in experimental glaucoma” by Zhong-Feng Wang (Fudan University). In a rat glaucomatous model, Dr. Wang found that increased intraocular pressure changed Kir4.1 currents and activated Muller cells that released inflammatory cytokines to evoke neuronal apoptosis (Gao et al., 2015). The findings based on this readily accessible model for *in vivo* studies left

a strong impression on the audience and its potential for treatment of glaucoma was appreciated.

The last talk was delivered by Yu-Feng Wang (Harbin Medical University). Glial fibrillary acidic protein (GFAP) is a type III intermediate filament and the major component of astrocytic cytoskeleton. In many degenerative, inflammatory and traumatic brain diseases, abnormal expression of GFAP has been identified; however, GFAP was still viewed as a simple maker of astrocytes. To explore the functional role of GFAP in astrocytic functional plasticity, Wang's team linked GFAP with other astrocytic proteins and identified their common spatiotemporal association during environmental challenges and then put forward a hypothesis of "Elastic retraction and extension network model" to explain the "guide role" of GFAP in astrocytic plasticity (Wang & Parpura, 2018). This proposal also triggered the thoughts of many young investigators on how to create new ideas in the study.

Others

Along with the 25 speakers, more other 10 other scholars also presented their works in glial studies. In addition, the meeting introduced two prosperous neuroscience journals, the *Neuroscience Bulletin* and *ASN Neuro*, which provided the participants excellent platforms to publish their works.

Concluding Comments

In the closing ceremony, Jia-Wei Zhou (Chairman of the Chinese Society of Neuroscience Glia Branch) summarized that the presentations represented the highest achievements of Chinese scholars on glial cells and promoted the cooperation between peers. The participants conducted extensive academic exchanges on the latest glial research and experimental techniques in and out of the meeting and familiarized themselves with the frontiers of glial studies. He specifically highlighted the contributions of the younger investigators who constituted roughly 75% of the attendees. As discoveries of glia in health and disease continue to emerge, members of the community all look forward to the next meeting that takes place in 2020.

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