SCIENCE CHINA
Life Sciences

• INSIGHT •

December 2011 Vol.54 No.12: 1156–1159
doi: 10.1007/s11427-011-4261-z

A brief review on current progress in neuroscience in China

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Received November 3, 2011; accepted November 15, 2011

Citation: Qiang M, Wu B B, Liu Y. A brief review on current progress in neuroscience in China. Sci China Life Sci, 2011, 54: 1156−1159, doi: 10.1007/s11427-011-4261-z

Neuroscience has been undergoing a rapid development in China since the beginning of the 21st century. Chinese scientists are working on neuroscience and getting more and more important results. As described by Poo Mu-ming [1], the increasing funding support, the flood of returning overseas researchers and numerous international conferences held in China give birth to the springtime of neuroscience in China.

The development of nervous system and neural cells

The nervous system is a complex network of axonal projections and synaptic connections [2]. At the early stage of neural development, besides generation of neurons and glial cells, synapse formation is the foundation of neuronal circuits and the basis of functions of nervous system including learning and memory.

Chinese neuroscientists have paid attention to neural development, especially to the cellular and molecular mechanisms of synaptic plasticity and neuronal plasticity [3]. Some of these studies highlight the research of synaptic plasticity, including elucidating the mechanism of actin polymerization-dependent maturation/regulation of presynaptic transmitter secretion, which appears significant for activity-dependent synaptogenesis and the plasticity of the synaptic network during development [4], indicating the role of hippocampal synaptic plasticity as a key factor in the effects of stress or glucocorticoids on opiate addiction [5]. Meanwhile, a lot of work on LTP/LTD regarded as a cellular basis for learning and memory was introduced [6]. According to Poo and colleagues, late-LTP which requires NMDA receptor activation is linked to long-term memory formation *in vivo* [7]. To elucidate the progress in synapse formation, the research of neuromuscular junction to excitatory central nervous system (CNS) synapses has been carried out, in addition with the mechanism exploration of activation of silent synapse in early development and investigation of synapse protein structure [8]. The role of transient receptor potential canonical (TRPC) channels in nervous system was investigated by Wang and colleagues. They found that TRPC channels mediate the role of brain-derived neurotrophic factor (BDNF) in promoting neuronal survival [9] and TRPC6 is involved in synaptic and behavioral plasticity [10].

In axon guidance and neuronal migration research [11], a hypothesis of chemotropic guidance of cortical radial migration [12] was supported by that semaphorin-3A is required as a chemoattractant for radial migration [13]. Calcium has been shown to play several roles in neuronal migration by mediating repulsive guidance, coordinating the changes in motility of growth cone and soma [14,15]. Meanwhile, Chung and Yuan reported that other molecules such as proteoglycans and rho GTPase are vital in mediating axon guidance and neuronal migration [16,17].

Study on ion channels and neurotransmitters

Ion channels could mediate rapid changes in membrane potential of synaptic transmission and be essential for a variety

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of neuronal functions, including neuronal survival. Chinese researchers contribute to find importance of ion channels in neuronal survival, for instance, Ca^{2+} influx induces neuronal damage via acid-sensing ion channels (ASICs) and kainate receptors, whereas leads to neuronal protection via L-type voltage-gated Ca^{2+} channels and TRPC 3/6 [18].

A noticeable result from the recent work of Rao and colleagues proved that neurotransmitters also have vital effect in social behavior. They have found that neurotransmitter 5-hydroxytryptamine (5-HT) is required for male mice in their sexual preference to male [19]. Other reports by Wang and coworkers show that action potential bursts enhance transmitter release at a giant central synapse and striatal dopamine release captures presynaptic action potential pattern information through different releasable pools [20,21].

Glial cells and the neural stem cells

In general, the central nervous system contains two major cell types, neurons and glial cells [22]. Duan summarized progresses in glial cell studies of several laboratories in China including his own work [23], which is concentrated on the mechanisms of neuron-glia crosstalking and glial cells' active roles in various brain functions and brain disorders. There are some worth noting results including that vesicle release was found in astrocytes [24] and neuron-glia signaling underwent activity-dependent plasticity similar to that found at neuronal synapse [25,26], olfactory ensheathing glial cells (OECs) secret some factors may attract neural stem/progenitor cells toward the lesion sites after OECs transplantation [27]. These studies support the viewpoint that glial cells play more roles than providing an ideal environment for neuronal cells as considered before [28]. Besides, Liu and colleagues found that small vesicles support glutamate release from astrocytes [29]. A method of selectively activating astrocytes in the mix culture of neuron and astrocyte was also established [30].

Embryonic and adult neural stem cell (NSCs) research is another hot spot in neurobiological research in China. A lot of work has been devoted to understanding the developmental regulation of NSCs and the application of NSCs in neurogenesis and neural regeneration [31]. It was revealed that brain injury did not alter the intrinsic differentiation potential of adult neuroblasts. Some molecules have also been identified as novel regulators of these processes. For example, aquaporin-4, an important molecule for maintaining water and ion homeostasis, was found to be a key factor during adult NSCs proliferation, migration and differentiation [32]. Protocadherin 18b, a member of Ca^{2+}-dependent cell adhesion molecules, was found involved in embryonic neurogenesis in *Zebrafish* [33]. Shen and coworkers have combined high-throughput screen with a random siRNA library on murine P19 cell differentiation toward neuronal lineage, as the first trail of new resource to seek new agents for directed neuronal differentiation [34]. With the development of patch clamp technique, function directed differentiation of NSCs is becoming a possible task and drawing more and more attention [35]. The application of neural stem cells in clinical treatment searching for cure of brain diseases is hopeful but has a long way to go.

The mechanism of sensory system and cognitive behaviors

The visual sensory system has long been investigated in China, and Chinese neuroscientists contribute a lot to understand the neural mechanism of the contextual effect, origin of the orientation selectivity and visual feature binding [36]. Take the advantage of *Drosophila,* a classical simple animal model which shares certain features of visual cognition in common with mammals at the genetic, molecular, cellular, and even higher behavioral levels, Guo and colleagues have got a series of important findings on the cognitive behaviors as well as learning and memory [37]. They gave the first report about the interaction between 'what' and 'where' pathways in *Drosophila.* Later, they also found that olfactory memory has been assigned to the mushroom body and the median bundle which were involved in visual pattern memory, therefore found a way to unveil the mystery of visual-olfactory memory integration mechanism. Another important progress from *Drosophila* was recently obtained on the molecular mechanism of social activities. Dopamine (DA) has been demonstrated to be crucial for decision making while increased dopamine level enhances male-male courtship in flies.

Some other investigations have tried to reveal the neural mechanism of vision-related cognitive functions at the cellular level, and have elucidated the role of two pairs of neurons in the central nervous system which control *Drosophila* initiate light preference [38], contrast pattern and contrast adaption of perceptual learning and temporal and spatial patterns of retinal ganglion cells in response to natural stimuli [39–41], sexual difference of aging-associated functional degradation in visual cortical cells [42].

In auditory system research, Shen and colleagues have presented the first data on the vocalizations of large odorous frogs (*Odorrana graminea*) accompanied by identifying ultrasonic calls as one of them. Their investigation also displays that ultrasonic frogs (*Odorrana tormota*) have extraordinary sex differences in auditory frequency sensitivity and show hyperacute phonotaxis to female courtship calls [43–45].

Pain, mainly as a result of chronic inflammation in nervous system, has different information pathway and pathological mechanism in sensory system. Zhang and coworkers have got great progress to reveal the molecular, cellular and neural circuit mechanisms of pain [46]. For instance, both the binding site and the immunolabeling of δ-opioid receptors (DORs) are shown to distribute in C- and Aδ-fibers in the

spinal laminas I–II, the protein kinase D1 and Cdk5 are involved in the generation of hyperalgesia of inflammatory pain [47,48], the activation of the NMDA receptor-PKA-ERK-CREB pathway is necessary for the induction of pain-related negative emotion [49]. They emphasize that the application and mechanism underlying acupuncture analgesia remains a subject of special interest for Chinese pain researchers.

The pathological mechanism of neurodegeneration

Neurodegenerative diseases are common disorders of the central nervous system, including Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), amyotrophic lateral sclerosis (ALS) and prion disease, which are characterized by progressive and irreversible neuronal loss in CNS [50]. More and more senior people suffer from AD and PD which are the most prevalent diseases in China [51]. Increasing studies show that neurodegenerative diseases have common cellular and molecular mechanisms including protein aggregation and inclusion body formation. A great many of Chinese researchers are interested in the research on neurodegenerative disorders in different aspects such as etiology, molecular mechanism of pathology, diagnosis and treatment. Molecular mechanisms of AD including protein aggregation, tau phosphorylation, and activation of glycogen synthase kinase-3 (GSK-3) have been elucidated. A super-sensitive assay to measure the level of the hyperphosphorylated tau for diagnosis of AD was developed by Wang [52]. In PD model, 6-OHDA lesioning was found to induce a relatively slow but sustained up-regulation of cystatin C, which exerted a neuroprotective action on DA neurons both *in vitro* and *in vivo* [53]. Chinese herbs' utility in treatment of AD and PD is uniquely studied [54].

Investigation of the relationship between endogenous formaldehyde and memory decline is currently carried out in China [55–57]. He and colleagues have found that the concentration of urine formaldehyde is related to senile dementia, and named the bifacial effect of formaldehyde in learning and memory "formaldehyde stress" [58]. Thus, the chronic impairment of memory-related nervous system from "formaldehyde stress" is hypothesized as one of the important pathogens for age-related dementia. Several genes such as DJ-1, LRRK2 and proteins including Parkin and PINK1 are related to PD pathology. The effects of these molecules were discussed in recent work of Chinese neuroscientists [59–62].

Computational neuroscience in visual and learning research

Computational neuroscience is a quickly developing subfield of neuroscience that uses mathematical methods to simulate and understand the function of the nervous system. Combined with neuroscience, computer science, physics and applied mathematics together try to explain how electrical and chemical signals are used in the brain to represent and process information [63]. As described by Wu and Liang, the history of computational neuroscience research in China began in 1959 which was a little late but went through rapid development in recent 10 years [64]. Chinese neuroscientists' work covers visual information processing, spatial and temporal information integration in receptive fields, motion detection, active vision, population and spatial-temporal coding in visual systems. Using computational approaches, Liang revealed that retina processes the visual information by both adaptation and the population coding operations. In 2011, using a simple linear integrate-and-fire model, Wu and colleagues investigated the effect of noise on accelerating computation and found that stimulus-dependent noise has better effect on speeding up network computation [65]. Guo and coworker adopted a computational modeling approach to identify how different brain areas and the dopamine system work together to drive a fly to make a decision, their results account well for experimental data [66]. Due to the accelerating development of neuroscience research in recent years, Chinese scientists have great confidence to obtain greater progress in this field in the near future.

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