It is estimated that more than 1 million Chinese people sustain traumatic brain injury (TBI) annually, nearly 10% of whom are dead and 30% are complicated with physical, cognitive, behavioral and/or psychosocial impairments in China. A lot of experimental researches and clinical trials of head trauma have been made in China recently, which improves the understanding of pathological mechanisms and prognosis of severe traumatic brain injury.

Guidelines for treatment of head trauma in China
Since "the Guidelines for the Management of Severe Traumatic Brain Injury" (the first, second and third editions) have been published in USA, more and more neurosurgeons have applied the guidelines to treat severe traumatic brain injury in China. More than 13,000 neurosurgeons in over 3,000 hospitals are qualified to clinically treat head trauma patients in China. Chinese Neurosurgical Association (CNA) started to set up the Chinese guidelines for diagnosis and treatment of head trauma 10 years ago, and recently published the book entitled "Chinese Guidelines for Diagnosis and Treatment of Head Trauma". CNA is promoting all neurosurgeons to learn and apply the guidelines to treat head trauma patients, especially for severe traumatic brain injured patients in China. The guidelines for management of severe traumatic brain injury have been widely applied in Shanghai, Tianjin, Beijing and eastern areas of China. However, it is certainly essential to promote the application of the guidelines in western and middle areas of China. The experts of CNA are travelling to different areas of China and giving lectures on how to correctly apply guidelines to treat the patients with head trauma. Hopefully, more and more Chinese neurosurgeons will accept the guidelines in the future in order to improve the clinical outcome of patients with head trauma in China.

Mild to moderate hypothermia for treatment of patients with severe traumatic brain injury in China
Mild to moderate hypothermia as a treatment of brain injury has been a major concern of research during the last decade. Laboratory studies have shown that mild to moderate hypothermia (at 32-35°C) has a significant protective effect, diminishes the neural damage, reduces the mortality as well as improves neurological outcome. Since 1990s, more than 30 clinical trials of mild-to-moderate hypothermia have been applied to treat over 1,000 patients with severe TBI in USA, Europe, Japan and China. Most of clinical findings suggest that mild hypothermia may improve the outcomes of severe traumatic brain injured patients with intracranial hypertension when cooling is maintained for over 48 hours, even it is not conclusive. Chinese neurosurgeons at Shanghai Renji Hospital and Tianjin Huanyu Hospital are the first group to apply long-term mild hypothermia (>48 hours) for treatment of severe traumatic brain injured patients in the world. Furthermore, mild hypothermia significantly decreases ICP values when refractory intracranial hypertension can not be controlled by conventional measures in patients with severe traumatic brain injury. However, prolonged mild to moderate hypothermia may be associated with high incidence of pneumonia and hypokalemia which should be prevented. Some clinical trials have not shown any therapeutic effect of mild to moderate hypothermia in severe traumatic brain injury, which may be related to the delayed cooling time after trauma, short duration of cooling, and fast rewarming speed of mild to moderate hypothermia.
Standard trauma craniectomy for massive cerebral contusion and refractory intracranial hypertension

Refractory intracranial hypertension caused by massive cerebral contusion, intracerebral/subdural hematoma, and brain edema in patients with severe traumatic brain injury is still the most important prognostic factor for such patients. However, the optimum technique for surgical decompression for refractory intracranial hypertension caused by severe head injury remains a subject of controversy. The American Association of Neurological Surgeons (AANS) considers decompressive craniectomy as one of several "second-tier therapies" for refractory intracranial hypertension resulting from severe TBI. Yet some neurosurgeons have recently confirmed the usefulness of decompressive craniectomy, and recommended it as the procedure of first choice for refractory intracranial hypertension in severe head injury. This raises the question of whether standard trauma craniectomy (STC) or limited craniectomy (LC) is the most effective technique for decompressive craniectomy in such cases. Unfortunately, a review of the literature does not provide a definitive answer. Nevertheless, in China and other countries, LC has remained the predominant surgical technique for treating severely head-injured patients with refractory intracranial hypertension. Therefore, it is essential to compare the efficacy of STC and LC for severe traumatic brain injury with refractory intracranial hypertension and massive cerebral contusion. Chinese neurosurgeons have made a series of clinical trials including Shanghai Renji Hospital, Guangzhou Nanfang Hospital, Tianjin Wujin Hospital, and Zhejiang Zhuji Hospital. The results indicate that STC can significantly improve the outcome in severe TBI with refractory intracranial hypertension and massive frontotemporoparietal contusion with or without intracerebral or subdural hematoma. More and more Chinese neurosurgeons would like to use STC to treat surgically severe traumatic brain injured patients with massive cerebral contusion and refractory intracranial hypertension.

Neural stem cells transplantation for recovery of neurological functions in patients with severe traumatic brain injury

Neural stem cells (NSCs) provide the potential hope of neurological recovery for patients with severe traumatic brain injury. More and more laboratory data have confirmed that transplanted NSCs in cerebral parenchyma are able to differentiate into neurons and move to damaged areas, which may establish axonal connection with original neurons for restoring the neurological function of patients with cerebral damage. Some neurosurgeons have made clinical trials to explore its possibility and usefulness. Neurosurgeons at Shanghai Huashan hospital have recently performed NSCs transplantation in more than 20 cases of cerebral contusion and got marked neurological recovery after NSCs transplantation. However, its clinical trial of NSCs is discontinued right now. There are still some clinical trials of NSCs to treat patients with coma, paralysis and other neurological dysfunction following severe traumatic brain injury or stroke. Definitely, NSCs transplantation should not be used in clinic because of the following reasons: first of all, NSCs transplantation has not been permitted to treat patients by National Health Ministry; secondly, the differentiation of NSCs into neurons cannot be controlled well, and most of NSCs differentiate into gliacytes, which may cause glioma confirmed by laboratory study; thirdly, there is a shortage of tools and evidences to confirm morphological and functional roles of NSCs in human patients. So, more laboratory studies need to be done. It is a long way to go before recommendation of clinical application.

Early cranioplasty for cranial defect after decompressive craniectomy in patients with severe traumatic brain injury

Traditionally, cranioplasty is performed within 6 months after decompressive craniectomy in patients with severe traumatic brain injury. Recently, more and more Chinese neurosurgeons prefer early cranioplasty (1-3 months) instead of delayed cranioplasty (6 months) for patients with decompressive craniectomy. Chinese neurosurgeons at Guangzhou Nanfang Hospital, Shanghai Renji Hospital, and Tianjin Wujin Hospital have found that early cranioplasty may promote the recovery of consciousness and improve the neurological functions without any major complications. However, early cranioplasty may not be applied for severe traumatic brain injured patients with primary brain stem injury, GCS< 5, age>65 years or < 12 years, or infection of central nervous system.

Genomics and proteomics of brain tissue following traumatic brain injury

In order to explore the early transcriptional changes of hippocampus after TBI, neurosurgeons at Shanghai
Renji Hospital have made laboratory study and established fluid-percussion (F-P) brain injury model. Affymetrix rat genome 230 2.0 array was used to detect the gene expression profile of hippocampus in control group or brain injury group. Laboratory data showed that 159 transcribes in TBI group changed significantly (much more than 2 folds) as compared with the control group. Of those with identified gene ontology function category, 136 transcribes were up-regulated and 23 transcribes were down-regulated. Preliminary data suggest that early transcriptional changes of hippocampus, especially a large amount of up-regulated genes, detected after traumatic brain injury in rats may be related to secondary injuries after TBI. Furthermore, Neurosurgeons at Shanghai Renji Hospital have explored the differential protein expression levels of hippocampus in rats by proteomics technique between TBI group and control group. The total protein mixture extracted in protein lysate was separated with two dimensional differential fluorescence in-gel electrophoresis (DIGE). The differential protein spots were identified by matrix-assisted laser desorption ionization time of flight mass spectrometry (MS-TOLF). Laboratory data showed that 17 protein spots were found with statistically significant change. Fourteen products of protein spots were identified by mass spectroscopy and two of them were repeated. And the actual products of proteins were thirteen, including cytoskeletons, energy-related enzymes, nucleic acids synthetic proteins, oxidative and stress proteins, synapse function related proteins, intracellular signal transduction proteins, and other unknown proteins. These differential proteins may be related to the pathophysiological mechanisms of TBI. To understand complex protein-protein association and molecular pathways of post-brain injury may help us generate potential diagnosis and therapies.

Neurosurgeons in Tianjin General Hospital have analyzed the difference of gene expression profile between the traumatic and normal human brain and look for new molecular biological strategies to prevent and treat brain trauma. There were 87 common genes in those differentially expressed genes from traumatic brains as compared with the normal brain. Sixty genes were up-regulated and 27 were down-regulated. Among the up-regulated genes, 44 genes were categorized into 12 functional categories and the other 16 genes’ function was not be clarified yet. Among the down-regulated genes, 7 genes were categorized into 4 functional categories and the other 20 genes’ function remained unknown. Those functional genes were searched in PubMed. It was found that cd44, cc12, tieg, vegf, cd14, xbpl, egrl, rgs2, fos, il-lb, timpl, gadd45a, cdkn1a, cnn3 and sppl were once reported in the literature on brain trauma. And qRT and PCR confirmed the reliability of the chip data. New molecular biological strategies for treating brain trauma will be developed and certainly needs more exploration in the future.

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