Highlights for the 10th Annual Conference of the International Association of Neurorestoratology

Zhongju Shi1,§, Zhijian Wei1,§, Shiqing Feng1 (✉), Gustavo Moviglia2 (✉), Lin Chen3, Ping Wu4

1 Department of Orthopaedics, Tianjin Medical University General Hospital, Tianjin 300052, China
2 Center of Research and Engineer of Tissues and Cellular Therapy, Maimonides University, Buenos Aires 775(1405), Argentina
3 Department of Neurosurgery, Tsinghua University Yuquan Hospital, Beijing 100040, China
4 Department of Neuroscience and Cell Biology, University of Texas Medical Branch, Galveston, TX 77555-5302, USA
§ These authors contributed equally to this work.

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ABSTRACT
The 10th annual conference of the International Association of Neurorestoratology (IANR) was held on Sept. 28-30, 2017. Here main promising topics were summarized, such as, memorial of Professor Geoffrey Raisman—Life Honorary President of IANR, highlights which include cell transplantation, new mechanism and new technology, problems and challenges in the field of Neurorestoratology.

The 10th annual conference of the International Association of Neurorestoratology (IANR) was successfully held in the capital of Argentina, Buenos Aires, from September 28 to 30, 2017. The theme of this annual session is to promote the basic science, translational and clinical studies of neurorestoration. More than 300 experts from all over the world attended the conference. The conference also held the 4th Annual Raisman Youth Forum, where young neuroscientists presented their research work and discussed the future directions of neurorestoration. The conference gave a profound memorial to Prof. Geoffrey Raisman—Life Honorary President of IANR, who was deeply cherished his critical contribution to the establishment of the IANR. Prof. Almudena Ramon-Cueto gave a podium presentation entitled “Geoffrey Raisman, A life at the Frontiers of Neural Science”. All attenders feel deeply sad about the unfortunate loss of a great neuroscientist and a leader. Daqing Li, a British scientist and a PhD student and colleague of Prof. Raisman, further summarized the legendary career life of Raisman.

In memory of Prof. Raisman, the fourth IANR Council Board members unanimously approved the following motions: (1) to rename the Youth Forum on IANR annual conferences as the Raisman Youth Forum to encourage young scientists and physicians to follow...
Prof. Raisman’s footsteps in neurorestoratology research; (2) to establish the Raisman Neurorestoratology Foundation for supporting clinical multicenter neurorestorative therapeutic trials or studies; and award the winner of Raisman Youth Forum; and (3) to write an article for commemorating Raisman and publish it in the *Journal of Neurorestoratology*.

**Highlights I: Cell transplantation**

One of the highlights of this conference is the detailed discussion of cell transplantation for neurorestoration. Cell transplantation has been reported to restore the neurological function for patients with central nervous system injury. There are several kinds of cells used for cell transplantation therapy, including neural stem cells, embryonic stem cells, mesenchymal stromal cells, olfactory ensheathing cells, and Schwann cells among others. Cell transplantation may become an effective therapeutic approach for neurorestoration. In this conference, Prof. Gustavo Moviglia reported the effect of cerebrolysin on differentiation of neural stem cells, and the title of his talk is “Cerebrolysin as induce of effectors cells and neural stem cell differentiation”. Prof. Ping Wu reported her research on differential responses of human neural stem cells to Zika virus infection, and this topic aroused great interest among the participants. Prof. Xijing He focused on the effects of bone marrow-derived macrophages on neural stem cell to repair spinal cord injury (SCI). The internationally renowned neuroscientist, Prof. Wise Young, delivered a talk on the international effort of a multicenter clinical study using umbilical cord blood mononuclear cells to treat chronic complete SCI and lithium therapy for severe neuropathic pain. He found that cord cells restored walking, bladder and bowel function in patients with chronic complete SCI.

Prof. Kyoung Suok Cho discussed their studies on Schwann cell transplantation, and he reported that grafting Schwann cells could improve axonal growth and forelimb strength after severe cervical spinal cord contusion. He also cited the previous study of Prof. Shiqing Feng, which showed that combination of activated Schwann cells with bone marrow mesenchymal stem cells was a better cell strategy for repair after SCI in rats. Prof. Qun Xue found that B7-H4 was important for the biological characteristics of mesenchymal stem cells by controlling the proliferation, migration and immunomodulatory effects of these cells. Prof. Xue Yao reported that ferroptosis contributed to secondary injury of SCI, and iron chelator DFO promoted SCI repair through ferroptosis inhibition. Therefore, ferroptosis targeting may serve as a promising therapeutic approach for treating SCI. Prof. Liyan Qiao’s presentation outlined the clinical advances of cell-based neurorestorative strategies that offer the broadest range of potential treatments for stroke. Furthermore, Prof. Zhiguo Chen gave a talk on the cell therapy for Parkinson disease.

Prof. Almudena Ramon Cueto reported the identification of functioning axons at the injury site after transplanting olfactory ensheathing cell into the injured rat spinal cord. Followed by a presentation by Prof. Daqing Li who introduced a standardized way to culture olfactory ensheathing cell for autologous transplantation to treat SCI, Prof. Ying Li found that transplantation of cultured olfactory bulb cells could prevent abnormal sensory responses from dorsal root avulsion in the rat. Furthermore, Prof. Zuncheng Zheng found that long-term outcome of olfactory ensheathing cell therapy was safe and effective in the treatment of SCI. Therefore, olfactory ensheathing cell transplantation is recognized as a useful repair strategy in adult mammals with traumatic SCI.

**Highlights II: New mechanism and new technology**

Numerous studies have focused on elucidating the neurorestorative and pathophysiologic mechanisms of SCI and promoting axonal regeneration following injury. However, the in-depth mechanisms remain largely unknown despite of recent studies indicating some of the neurorestorative mechanisms such as reducing cell death, minimizing the extent of the injury, and facilitating axonal regeneration. Participants discussed on the new mechanisms and new technology of neurorestoratology in this conference. Prof. Jianzhong Hu reported his research on the effects and the mechanism of microRNA-21 in acute SCI repair. Prof. Hooshang Saberi reported on “Cytokines and Leukines to promote the natural recovery of spinal cord injury”. In recent years, tissue engineering-based approaches have been proposed as alternatives for SCI repair/regeneration. Prof. Hari Shakner Sharma presented his research on nanowired delivery of stem cells and neurolysin in reducing Alzheimer’s disease pathology. Prof. Liming Cheng combined with his
research and clinical experiences, and introduced the strategies in the repair of SCI by mobilizing endogenous neural stem cells. Prof. Qiang Ao reported “Repairing peripheral nerve injury with using acellular nerve materials". Prof. Gruarin Franco talked about the biomechanics of SCI caused by gunshot and the surgical treatment options. Prof. William Slikker reported “Pathways to protection from the effects of anesthetic-induced developmental neurotoxicity”. Prof. Siwei You discussed his study about the restoration of optic neuropathy. Prof. Frances Ciccetti gave a talk on “Prion-like propagation of mutant huntingtin protein: Implications for Huntington’s disease and other pathologies of the CNS”. About the exosome, Prof. Ashok Shetty suggested that exosome therapy might have potential for modulating epilepticus induced hippocampal dysfunction. Prof. Adina Stan introduced the clinic aspect of neurorestoratology. Prof. Raul Arizaga talked about the neurotrophic factors and neurodegeneration. Followed a wonderful talk by Prof. Ignacio Previgiano on the brain vascular dysfunction, Prof. Jose V. Lafuente reported the role of nanowired cerebrolysin in modulating pathophysiology of Parkinson disease and neurorestoration. Prof. Edgardo Alvarez presented the research on trace elements as epigenetic biomarkers of cognitive expression. Prof. Peng Liang introduced the concept of inosine in axon sprouting and motor recovery after SCI. Prof. Teresita Moviglia reported the research on the holistic treatment for chronic SCI patients. Prof. Ranjana Patanek talked about the relation between stroke and neurorestoratology. Prof. Xinli Ni found that apoptosis-inducing factor (AIF) nuclear translocation and neuronal cell death were associated with Iduna loss after severe hypoxic-ischemic (HI) in the immature brain. Prof. Anibal Grangeat introduced the treatment of intervertebral disc pathologies.

In terms of the advanced technology, Prof. Yong Hu demonstrated the use of resting state fMRI (rsfMRI) to study spinal cord connectome. He suggested that the functional connectivity analysis of human cervical spinal cord using rsfMRI could be a promising tool to identify the physiological function of spinal cord and the underlying pathophysiology of SCI. Exosomes play a key role in the intercellular communication and mesenchymal stem cell-derived exosomes can improve functional recovery and promote neuroplasticity in rats after TBI. Along this line, Prof. Michael Chopp reported on “Restorative Neurology using exosomes and microRNA tailored exosomes for the treatments of stroke, neural injury and neurodegenerative disease”. Prof. Lin Chen introduced the application of microvascular decompression (MVD) surgery for nerve repair. Prof. Sang Ryong Jeon presented his research on optogenetic stimulation for controlling dopaminergic neurons in a Parkinson rat model. Prof. Giovanni Tosi reported on “Nanomedicine and brain disorders and neurorestoration”. Prof. Qunyuan Xu discussed on application of magnetic nanoparticles in imaging of brain tumors. Prof. Gustavo Albanese and Prof. Damian Couto introduced the EMGAs reinervation neurological test. Prof. Pedro Lylyk reported on “Minimal invasive treatment for central neurosystem vascular pathology”. Prof. Yi Hong discussed the relation between neuromodulation and neurorehabilitation. Prof. H Mombasheri reported on “Manipulation of neural cell activities by biomaterials and biophysical approaches to repair the damages caused by SCI”. Prof. Xiaohong Wang found that the double-layer polyurethane-collagen conduit had a better nerve repair effect comparing to the pure PU conduit, and the 3D printed double-layer polyurethane-collagen conduit held the potential to be used in clinical for peripheral nerve repair. Prof. Kwan Ho Park gave a talk on the effect of trauma in osteoporotic vertebral compression fractures treated by percutaneous vertebroplasty.

**Highlights III: Problems and challenges in the field of Neurorestoratology**

The founding IANR president, Prof. Hongyun Huang, introduced the latest research advances and prospects of clinical therapeutics in neurorestoratology. He pointed out that the neurorestorative strategies mainly included cell therapy, neuromodulation via the brain-computer interface, restorative surgery, pharmaceutical or chemical therapies, biomaterials and bioengineering among others. Furthermore, he pointed out that the challenges included (1) to spread effective neurorestorative therapies, and (2) to make them as routine treatment to let patients to optimize functional neurorestoration. Neurorestorative therapies should be trialed as a multicenter effort, with randomized, double-blinded, placebo-control studies to promote an evidence-based medical practice. Currently Chinese Association of Neurorestoratology is organizing and carrying out series of cell therapies via multicenter...
randomized, double-blinded, placebo-control clinical studies for neural diseases and damages. Up to date, the preliminary results are consistent with the expectation. Prof. Alok Sharma talked about biomechanics of neurorestoratology, and praised the personalized ethics in Japan. The participants also get some insights from his presentation.

Prof. Shiqing Feng gave a presentation focusing on the “Problems and challenges in spinal cord injury”. He pointed out that the pathophysiologic characteristic of SCI is complicated, which includes at least three aspects. First, at the molecular level, SCI is usually accompanied with increased inflammatory factors and neurotrophin precursors. Second, at the cellular level, the endogenous neural stem cells show differentiation imbalance, and the mature central nervous system exhibits limited regeneration ability. Third, at the tissue level, one important inhibitive factor is glia scar forming and the activation of astrocytes. These three issues interact with each other to suppress neural regeneration. Then he illustrated that the microenvironment imbalance was the microenvironment suffering from the increase of inhibitive factors and the reduction of promotive factors after SCI, and he built a standard diagnosis and treatment procedure based on the epidemiological investigation and the microenvironment imbalance theory. Prof. Feng then touched the directions and challenges in the future. Firstly, the big data collection from individuals and establishment of database on multi-omics is necessary. Multi-center research is recommended globally to realize data sharing. At the molecular level, the key regulatory molecules should be found, and combined therapies will be a more effective strategy to promote recovery than a single approach. Cell transplantation therapy still holds the potential to promote repair and functional plasticity following SCI.

Raisman Youth Forum

The purpose of the forum is to provide young and highly motivated trainees, such as graduate students and postdoctoral fellows, an opportunity to present their exciting research projects as well as to improve the skills of scientific presentation and communication. Dr. Zhijian Wei made a speech about the proteomics analysis of Schwann cell-derived exosomes, which indicated a novel therapeutic strategy for SCI to replace traditional cell transplantation. Dr. Zhongju Shi explored the bio-function of miR-29a in neural stem cells and proved that miR-29a promoted the neuronal differentiation and decreased the astrocytic differentiation via modulating the PTEN/P13K/AKT signaling pathway. Dr. Wei Xu reported that genetically modified umbilical cord mesenchymal stem cells to overexpress BDNF could reduce local inflammatory responses, inhibit neuronal apoptosis, and decrease the demyelination and glial formation after cells transplanted into the injured spinal cord. Dr. Rongrong Zhu demonstrated a new approach of using NT3-loaded nanocomposites to regenerate spinal cord tissue, which promoted the microenvironment favoring the differentiation of endogenous neural stem cell and accelerated axonal re-growth. Dr. Wu Jiang revealed the latest progress in selectively inhibiting NLRP3 inflammasome activation after SCI, and found that blocking NLRP3 could attenuate mitochondrial dysfunction, microglia activation, neutrophils infiltration, and reactive gliosis and improve neurological recovery. Through the intense competition, Dr. Zhijian Wei (Tianjin, China) won the first prize for his report.

Board meeting of the fourth IANR council

The meeting of the fourth IANR council board was held on September 28, in which committee members prepared a work summary and the future development plans for IANR. This conference also accomplished several administrative tasks. First, the fourth IANR council board members were selected from potential candidates, which were approved by the Core Administration Committee. Second, it was agreed that Prof. Wise Young as the Chairman to organize the 11th IANR annual conference in the United States in October, 2018. Third, a motion was passed to establish the special committee on neural diseases or damage, or sub-discipline of Neurorestoratology. Fourth, IANR council board members were encouraged to explore or test new neurorestorative therapeutic strategies in both pre-clinic and clinic setting. Fifth, it was agreed to establish a neurorestorative therapeutic guideline for each different neural diseases or damage. Sixth, it was decided to choose the venue of the 12th annual conference on the next conference (potential places include Beijing, Shanghai, Jordan, or other Arab countries, Poland and Romania).