SPECIAL ISSUE

New era of treatment and evaluation of traumatic brain injury and spinal cord injury

Traumatic brain injury (TBI) and spinal cord injury (SCI) are leading causes of death and disability worldwide (Center for Disease Control, 2006). Both injuries are induced by external traumatic event and likely happen together. After the primary traumatic incident, the secondary injury, including ischemic, inflammatory, metabolic and biochemical cascades, is likely more devastating (Blumbergs, 1997). To date, all clinical trials have failed to cure TBI and SCI, due to the heterogeneous and complex nature of injury pathophysiology (Saatman et al., 2008). There is no single technique that can completely assess the pathophysiological profile of TBI or SCI. Similarly, we cannot expect one single drug to cure this complex phenomenon either. Thus novel approaches are needed for therapeutic development and evaluation. In this special issue, a collection of five succinct reviews summarized the state of the art research from injury detection to novel treatment. This collection also serves as the Proceedings of 2015 Chinese Neurotrauma Scholars Association (CNSA) Symposium held in July, 2014 in San Francisco, CA, USA. The authors are invited speakers at the symposium and also leaders in their respective fields. Instead of giving lengthy systematic reviews, the papers meant to summarize the current cutting edge development and offer meaningful insights of the field to layman readers.

At gross level, advanced magnetic resonance imaging (MRI) provides an excellent tool to capture the pathophysiological profile following TBI. Duong and Watts (2015) provided a summary of multi-parametric imaging approach to brain injury detection and longitudinal assessment. Among them, T1 provides structural information, T2 detects potential edema, and diffusion tensor imaging (DTI) identifies abnormalities in white matter tract integrity. In addition to neuronal and structural injury, the neural vascular system is also vulnerable to injury. However, MR evaluations of blood-brain barrier (BBB) break down and compromise of cerebral blood perfusion and cerebral vascular reactivity are still under investigated. Duong and Watts (2015) also offer insights in this direction. At molecular level, by using manganese as an MR contrast agent and also calcium analog, manganese-enhanced MRI (MEMRI) could reveal the molecular pathway of calcium in TBI pathophysiology. Down the road, a multi-parametric MRI approach will be a new standard of non-invasive assessment of brain injury in both animal models and human studies. In addition to injury detection, the identification of key signal pathways that mediate neuronal degeneration or even potential regeneration will likely to offer a novel treatment regimen. Wu and Xu (2015) summarized the role and mechanisms of RhoA/Rho kinase-mediated spinal cord pathogenesis and the potential of targeting RhoA/Rho kinase as a strategy for promoting neuroprotection and axonal regeneration.

In TBI/SCI treatment strategy, apart from the conventional approaches targeting certain pathophysiological pathways, neural transplantation or cell-based therapy could provide a novel treatment solution to repair and regenerate the injured central nervous system (CNS). Stem cells can be self-adaptive to the host environment providing multi-folded roles, from neuronal protection, neurotrophic effect to direct neuronal replacement to facilitate the repair and regenerative process of the injured CNS following TBI or SCI. Sun (2015) provided an excellent review of the cutting edge neural transplantation/cell-based therapy for brain repair and regeneration after TBI. The author provided insight views of the application of different cell types, from embryonic stem cells, adult neural stem cells, bone marrow stromal cells, and other types of stem or stem-like cells for TBI application, and pointed out the pros and cons of each cell type and the future directions of investigation. Among stem cell therapy, one of the most exciting developments in recent years is the somatic cell-derived neural stem cells or neurons by epigenetic reprogramming techniques. The so-called inducible pluripotent stem cells (iPSCs) are derived from adult cells and can come from patients themselves, thus avoiding ethical concerns and graft rejection issues. Since the discovery of iPSCs (Yu et al., 2007; Nakagawa et al., 2008), many new techniques have been developed to improve the proficiency in generating desired cell populations. The direct reprogramming of somatic cells into neural stem cells or neurons without the pluripotency stage provides a short cut not only reducing the time length to generate neural stem cells but also avoiding tumor formation. Hou and Lu (2015) summarized the most exciting development in this avenue and its potential for treating TBI and SCI. More interestingly, direct conversion of endogenous supporting cells into neuronal cells *in vivo* is also possible. Examples like glia can be directly converted to neurons by using proper transcription factors (Sun, 2005). Taken together, the reprogramming for conversion of somatic cell types into induced neurons or neural stem cells opens a new door for treating TBI and SCI (Hou and Lu, 2015). Meanwhile, *in vivo* assessment and characterization of transplanted cells including cell migration, distribution, differentiation and their roles in angiogenesis and neurogenesis are still challenges. High resolution MRI can be a viable tool to assess migration and distribution of transplanted cells. Cells labeled with iron oxide-based superparamagnetic nanoparticles can be detected by MRI *in vivo* non-invasively. The use of Gadolinium-DTPA based contrast agent offers means to assess vascular remodeling following cell transplantation. Jiang (2015) summarized the development of novel MR imaging of cell-based therapy at molecular level and also identified the problems to be resolved in the field.

In short, the technical advent of imaging and stem cell research offers unprecedented opportunities for researchers to re-look the old problems from fresh perspectives. There is no doubt that the findings on stem cell-based therapy in TBI or SCI just revealed a tip of the iceberg and numerous questions need to be answered before its clinical translation. However, the new discoveries today already demonstrated its potential as a viable solution. Together with non-invasive imaging techniques in both gross and molecular levels, they could open a new era of novel treatment and non-invasive assessment of TBI and SCI.

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