Treatment of Spinal Cord Injury Using Transplantation of Motoneurons Derived from Adipose Stem Cells Following Histone Deacetylases Inhibitors Therapy in Acute Phase

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Abstract
The majority of cases of spinal cord injury (SCI) occur during car crashes. SCI damages axons and disrupts sensory and motor neuronal transmission. The replacement of damaged neural cells in the injured CNS is limited. Although various treatment regimens can partially alleviate SCI, the mechanisms responsible for symptomatic improvement remain elusive. In this study, we transplanted motoneurons derived adipose stem cells with Valporic acid in animal model of SCI. Rats were divided into three groups: (1) laminectomy (without SCI) only; (2) laminectomy+ SCI+VPA (300 g/kg and 12h post injury); (3) SCI+motoneuron like cells (MNLCs) infused 7 days post injury+VPA (300 g/kg and 12h post injury). Contusion injury was performed with a New York University (NYU) weight-drop device. Locomotors function was assessed by the H-reflex and Basso-Beattie-Bresnahan (BBB) test for 12 weeks. Spinal cord was examined histologically, including size of cavitation, expression of glial fibrillary acid protein (GFAP) and axonal regeneration and position of cell replacement, three month after surgery. Open-field test scores of SCI rats which treated with MNLCs+VPA (300 g/kg and 12h post injury) were significantly improved compared to injured group ($P<0.05$). The cavity volume in the VPA+MNLCs group significantly reduced compared to control (saline-injected) group ($P<0.05$). The level of GFAP significantly decreased in the VPA treatment group, while it significantly increased in control ($P<0.05$). Together, our results demonstrated the neuroprotective property of VPA in the SCI model.

Keywords: Valproic Acid, Neuroprotection, Motoneuron, Histone Deacetylases, Spinal Cord Injury.

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