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Olfactory Mucosa Transplantation for Spinal Cord Injury

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Abstract

Carlos Lima et al. who are pioneers in this field reported their clinical pilot study of olfactory mucosa transplantation for chronic spinal cord injury. They showed the safety and feasibility of it. Olfactory mucosa contains the olfactory ensheathing cells and neural stem cells. Recent studies have demonstrated the potential therapeutic role of both cells in spinal cord injury. We have already reported the effectiveness of olfactory mucosa transplantation for rat spinal cord injury. Furthermore we indicated the reconstruction of cortico-spinal tract by BDA (biotinylated dextran amine) tracer study with the olfactory mucosa transplantation. We elucidated how grafts of nasal olfactory mucosa repair the injured rat spinal cord as compared with the nasal respiratory mucosa containing no olfactory ensheathing cell and neural stem cell. The spinal cord of recipient rats (adult female Sprague-Dawlley rats; 10 rats; 160-180g) was exposed at The 8-9 level, and a contusion injury was produced using the weight drop device developed at New York University. The exposed cord was moderately contused by a 10g weight that dropped from a height of 75 mm. A couple of weeks after injury, the injury site were exposed and posterior sulcus of the spinal cord was opened. Minced olfactory mucosa or respiratory mucosa derived from GFP rats were transplanted into the sulcuses. The BBB score in each animal was observed at 1, 2, 4 and 8 weeks after the transplantation. The recovery of the hind limb movement in the olfactory mucosa transplanted rats improved significantly compared to the respiratory mucosa transplanted rats. In histological assessment, the expression of p75NGFR and GFAP was strong in the olfactory mucosa grafts at 1 and 2 weeks after the transplantation and it was decreased at 8 weeks after the transplantation. The expression of p75NGFR and GFAP was not observed in the respiratory mucosa graft. The expression of Neurofilament was observed strongly at the site in the olfactory mucosa transplanted rats. The numerous fibres strongly stained with Neurofilament were surrounding the GFP positive cells and penetrating the transplanted olfactory mucosa. There were no apparent Neurofilament stained fibres at the marginal spinal cord. As we have already reported, olfactory mucosa transplantation for spinal cord injury has a certain effectiveness for the hind limb motor recovery. In this study, we recognized the numerous axons which surround the transplanted cells and penetrate the mucosa at the transplanted site without marginal spinal white matter. Olfactory mucosa might be more suitable niche than white matter which contains inhibiting factor for axonal regeneration in spinal cord. To succeed the neuronal regenerative therapy, cells, factors and scaffold have been required. Olfactory mucosa might have all of them. We are now performing the clinical trial of olfactory mucosa transplantation for chronic complete spinal cord injuries in Japan. We could have four patients so far and recognize the voluntary EEG of their thigh.

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