Functional improvement of focal cerebral ischemia injury by subdural transplantation of induced pluripotent stem cells with fibrin glue.

Authors: Chen S.-J., Chang C.-M., Tsai S.-K., Chang Y.-L., Chou S.-J., Huang S.-S., Tai L.-K., Chen Y.-C., Ku H.-H., Li H.-Y., Chiou S.-H.

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Abstract:

Ischemic stroke is the leading cause of disability in the world. Cell transplantation has emerged in various neurological diseases as a potential therapeutic approach in the postacute stroke phase. Recently, inducible pluripotent stem (iPS) cells showed potential for multilineage differentiation and provide a resource for stem cell-based therapies. However, whether iPS transplantation could improve the function of stroke-like model is still an open question. The aim of this study is to investigate the therapeutic effects of subdural transplantation of iPS mixed with fibrin glue (iPS-FG) on cerebral ischemic rats induced by middle cerebral artery occlusion (MCAO). We demonstrated an efficient method to differentiate iPS into astroglial-like and neuron-like cells which display functional electrophysiological properties. In vivo study firstly showed that the direct injection of iPS into damaged areas of rat cortex significantly decreased the infarct size and improved the motor function in rats with MCAO. Furthermore, we found that the subdural iPS-FG can also effectively reduce the total infarct volume and greatly improve the behavior of rats with MCAO to perform rotarod and grasping tasks. Importantly, analysis of cytokine expression in iPS-FG-treated ischemic brains revealed a significant reduction of pro-inflammatory cytokines and an increase of anti-inflammatory cytokines. Taken together, these results suggest that iPS cells could improve the motor function, reduce infarct size, attenuate inflammation cytokines, and mediate neuroprotection after ischemic stroke. Subdural iPS-FG could be considered as a more safe approach because this method can avoid iatrogenic injury to brain parenchyma and enhance recovering from stoke-induced impairment.