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TRANSPLANTED IMMORTALIZED NEURAL STEM CELLS INTO THE INJURED SPINAL CORD PROMOTE A RECOVERY OF VOIDING FUNCTION IN THE RAT

Aims of Study

Little spontaneous neural regeneration occurs following spinal cord injury (SCI). However, axonal regrowth and functional neural recovery have been accomplished by transplantation of certain cells into the injured spinal cord.[1)] In fact, several articles reported that transplantation of neural stem cells and genetically modified cells to express neurotrophic factors into the injured spinal cord improved a gait function to some extent.[2), 3)] In this study, we transplanted EG6 cells, which are immortalized neural stem cells, into the injured spinal cord of the rat and investigated a functional recovery of the lower urinary tract.

Methods

Female Wistar rats were used. Following halothane inhalation, laminectomy was performed at Th8/9 and SCI was created by compression with 40 gm rod placed on the exposed dura for 30 min. Bladders were manually expressed twice daily following SCI. EG6 cells (10^6 / 10micro l) pre-labeled in vitro with BrdU (100 micro M) were transplanted into the injured spinal cord under halothane inhalation at the 9th day after SCI. Control rats received intraspinal injections of culture medium alone as vehicle. Beginning on the day of intraspinal injection of EG6 cells or vehicle, SCI rats received an immunosuppressive agent FK-506 (0.5mg/kg, subcutaneously) daily. To evaluate bladder function, voiding behavior in a metabolic cage was observed for 24 hrs on the 14th and 28th day after transplantation. Voided volume per micturition was compared between control and EG6-treated rats. For cystometry, polyethylene catheter was introduced into the bladder under halothane inhalation on the 28th day after transplantation. Two hrs after the bladder catheter placement, when rats recovered completely from halothane anesthesia, saline was infused into the bladder via the catheter at the rate of 0.2 ml/min. Intravesical pressure was recorded to compare urodynamic parameters between control and EG6-treated rats. After cystometry, rats were sacrificed and the spinal cord was removed to identify transplanted EG6 cells using an immunohistochemical technique.

Results

Transplanted EG6 cells with immunoreactivity to BrdU were identified on the 28th day after transplantation. In the analysis of voiding behavior, voided volume per micturition significantly increased in EG6-treated rats (1.45 $\pm$ 0.29 ml [n=6]) compared with control (0.85 $\pm$ 0.49 ml [n=6]) on the 28th day, ($P<0.05$), but not on the 14th day (control: 0.72 $\pm$ 0.37 ml [n=7] vs EG6: 0.97 $\pm$ 0.36 ml [n=7]) after transplantation. In cystometry, micturition pressure significantly decreased in EG6-treated rats (23.2 $\pm$ 4.2 mmHg [n=7]) compared with control (39.0 $\pm$ 7.4 mmHg [n=5]) ($P<0.005$). Although voided volume was not different (control: 0.94 $\pm$ 0.30 ml [n=5] vs EG6: 1.13 $\pm$ 0.22 ml [n=7]), postvoid residual was significantly smaller in EG6-treated rats (0.94 $\pm$ 0.75 ml [n=7]) than control (3.14 $\pm$ 1.84 ml [n=5]) ($P<0.05$). Thus, voiding efficiency was significantly higher in EG6-tretaed rats (60.7 $\pm$ 19.8% [n=7]) than control (27.9 $\pm$ 16.6% [n=5]) ($P<0.05$). Detrusor hyperreflexia was noted in 3 of 5 control rats (60%) and 4 of 7 EG6-treated rats (57%).

Conclusions

Transplanted EG6 cells into the injured spinal cord can survive for at least 4 weeks and promote a recovery of voiding function. Further study will be needed to determine the factors responsible for the benefit seen here. Neural stem cells transplantation seems to be a promising modality for the treatment of lower urinary tract dysfunction following SCI.

References:

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