Title:

Replacement of hematoma with neural progenitor cells embedded in a nanomaterial in a rat model of intracerebral hemorrhage

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Abstract:

Background and purpose

To reconstruct the injured brain tissue, cell replacement therapy has been extensively studied in brain injury and neurological diseases. Following intracerebral hemorrhage (ICH), hematoma removal reduces perihematomal edema. In this study, the effect of transplanting neural progenitor cells (NPCs) seeded in a self-assembling peptide (SAP) solution into the hematoma cavity following hematoma aspiration on functional recovery and the underlying mechanism were investigated in a rat model of ICH.

Methods

Brains from embryonic day 13.5 embryos of green fluorescent protein (GFP) transgenic SD rats were dissected and processed for neural progenitor cell (NPC) culture. ICH was induced in adult Sprague-Dawley rats by an intrastriatal injection of bacterial collagenase IV. Hematoma aspiration was done at 3.5 h after ICH onset. NPCs in SAP solution, or medium in SAP solution, or medium alone, was injected into the cavity immediately following hematoma aspiration. The functional outcome was assessed till 2 weeks after ICH using modified limb placement test (MLPT) and neurological severity score (NSS). The survival and differentiation of the NPCs were assessed using immunofluorescent staining. The expression of neurotrophic factors in the lesion site was evaluated using ELISA.

Results

The cells group exhibited a slightly better performance, according to MLPT and NSS, than control groups at 14 days after ICH. A small proportion of NPCs within the SAP scaffold survived at 2 weeks after transplantation. More than half of the survived cells remained undifferentiated with expression of nestin, while a quarter of the cells differentiated into GFAP positive astrocytes. Only a very small proportion of GFP cells were NeuN positive neurons. The cells group showed a trend toward an increased secretion of neurotrophic factors, including NGF, BDNF, GDNF and NT-3. However, this did not reach the significant level compared with the control groups.

Conclusions

Transplantation of NPCs embedded in the nanomaterial into the hematoma cavity improved functional recovery. NPCs could survive in the nanomaterial and partially differentiate into specific neural cells. This study may provide evidence for a new therapeutic strategy for ICH. However, further study on modulation of the microenvironment is needed to improve the survival of the transplanted cells.