Long-term benefit of human fetal neuronal progenitor cell transplantation in a clinically adapted model after traumatic brain injury.

Abstract:
Experimental human fetal neural progenitor cell (hfNPC) transplantation has proven to be a promising therapeutic approach after traumatic brain injury (TBI). However, the long-term efficacy and safety, which are both highly important for clinical translation of this approach, have thus far not been investigated. This study investigated the effect of local (L, $1 \times 10^5$ cells) and systemic (S, $5 \times 10^5$ cells) administration of PKH-26-labeled pre-differentiated hfNPCs over a period of 12 weeks, beginning 24 h after severe controlled cortical impact TBI in Sprague-Dawley rats. Accelerating rotarod testing revealed a trend toward functional improvement beginning 1 week after transplantation, and persisting until the end of the experiment. The traumatic lesion volume as quantified by magnetic resonance imaging was smaller in both treatment groups compared to control (C) animals (C = 54.50 mm$^3$, L = 32 mm$^3$, S = 37.50 mm$^3$). Correspondingly, neuronal (NeuN) staining showed increased neuronal survival at the border of the lesion in both transplanted groups (S = 92.4%; L = 87.2%; 72.5%). Histological analysis of the brain compartments revealed transiently increased angiogenesis and reduced astroglial reaction during the first 4 weeks post-transplantation. PKH-26-positive cells were detected exclusively after local transplantation.
without any evidence of tumor formation. However, graft differentiation was seen only in very rare cases. In conclusion, transplantation of hfNPCs improved the long-term functional outcome after TBI, diminished trauma lesion size, and increased neuronal survival in the border zone of the lesion. This therapeutic effect was not likely due to cell replacement, but was associated with transiently increased angiogenesis and reduced astrogliosis.