

## Neurologically impaired mice improve after receiving human stem cells

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Scientists report a dramatic success in what may be the first documented rescue of a congenital brain disorder by transplantation of human neural stem cells. The research, published by Cell Press in the June issue of the journal *Cell Stem Cell*, may lead the way to new strategies for treating certain hereditary and perinatal neurological disorders.

Nerve cell projections are ensheathed by a fatty substance called myelin that is produced by oligodendrocytes, a type non-nerve cell in the brain and spinal cord. Myelin enhances the speed and coordination of the electrical signals by which nerve cells communicate with one another. When myelin is missing or damaged, electrical signals are not properly transmitted.

Previous studies have explored the potential utility of cell transplantation for restoring absent or lost myelination to diseased nerve fibers. Much of this research has made use of the 'shiverer mouse' animal model which lacks normal myelin and typically dies within months of birth. Yet to date, no transplantation of human neural stem cells or of their derivatives, called glial progenitor cells, have ever altered the condition or fate of recipient animals.

Dr. Steve Goldman and colleagues from the Departments of Neurology and Neurosurgery at the University of Rochester Medical Center, along with collaborators at Cornell, UCLA and Baylor, built on this earlier work by devising a more robust method for the acquisition and purification of human fetal glial progenitor cells.



In addition, they developed a new cell delivery strategy, based on multiple injection sites, to encourage widespread and dense donor cell engraftment throughout the central nervous system of recipient mice. The researchers transplanted human glial stem cells into neonatal shiverer mice that also had a genetically deficient immune system. Immunodeficient mice were used to minimize the rejection of the transplanted cells.

The researchers found that the new transplant procedure resulted in infiltration of human glial progenitor cells throughout the brain and spinal cord. The engrafted mice exhibited robust, efficient and functional myelination. Most notably, many of the mice displayed progressive, neurological improvement and a fraction of the mice were actually rescued by the procedure. "The neurological recovery and survival of the mice receiving transplants was in sharp contrast to the fate of their untreated controls, which uniformly died by five months," explains Dr. Goldman. Upon histological examination well over a year after the procedure, the white matter of the surviving mice had been essentially re-myelinated by human cells.

"To our knowledge, these data represent the first outright rescue of a congenital hypomyelinating disorder by means of stem or progenitor cell transplantation," offers Dr. Goldman. "Although much work needs to be done to maximize the number of individuals that respond to transplantation, I think that these findings hold great promise for the potential of stem cell-based treatment in a wide range of hereditary and ischemic myelin disorders in both children and adults."

Source: Cell Press

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